BRAIN.

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Original Articles and Clinical Cases.

ON THE CERVICAL SPINO-BULBAR AND SPINO-CEREBELLAR TRACTS AND ON THE QUESTION OF TOPOGRAPHICAL REPRESENTATION IN THE CEREBELLUM.

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Introduction.

The object of the following investigation was to establish, if possible, what tracts ascend from the cervical region of the spinal cord to the bulb and to the cerebellum, for it is curious that hiatuses yet exist in our precise knowledge of the tracts which pass from the spinal cord to the cerebellum, one of the most notable being the absence of investigation into the relation of the spinal innervation of the fore-limb to the cerebellum. Indeed, as regards the spinal cord itself, practically the only attempt to compare the proportional representation of the fore- and hind-limb respectively in the spino-cerebellar paths is contained in the paper by Collier and Buzzard (*vide* Table A, p. 242). In the present work the examination of our material has also afforded an opportunity of considering how far anatomical research supports the views on the localization of function in the cerebellum which have been especially advanced by van Rijnberk on the anatomical ideas of Bolk.

As regards the first of these questions, while the source of the direct tractus spino-cerebellaris dorsalis is fairly well recognized and its destination partly ascertained, the origin of the tractus

spino-cerebellaris ventralis, Gowers' tract, is almost as unknown to-day as when Edinger said of it in 1904 "der Ursprungsort ist noch nicht bekannt."

Its terminal distribution also to the vermis cerebelli, first ascertained by Mott, has since been variously described and requires fresh determination. Further, the origin and destination of the marginal fibres between these two great tracts and which compose the dorso-ventral tract of Pellizzi have received little attention, except from that author.

Our anatomical results will be classified according to each of these tracts in their dorsal and ventral order, but chiefly according to the metameric level of the cord from which the fibres arise. For this purpose, we may draw attention to the arrangement of the motor functions of the spinal cord which are in part subserved by the spino-cerebellar arcs of which Flechsig's and Gowers' tracts constitute the afferent side.

Arrangement of the Motor Representation of the Trunk and Limbs in the Spinal Cord.

Though the spinal cord must be regarded as a segmental mechanism, it is also the seat of special groupings of nerve centres (Goltz, Sherrington, Lapinsky) innervating the musculature for movements of the head and neck, of the fore-limb, the trunk and the hind-limb. It is the association of such compound central mechanisms with the cerebellum that is subserved by the spino-cerebellar paths, and therefore it appears to us that the afferent impressions to the small brain may be considered as originating in one or other of the following regions:

Region I	1 C. to 4 C.	Rotation of head and neck	}	Flexion, extension, lateral adduction of head and neck.
Region II	5 C. to 1 D.	Fore limb		
Region III	2 D. to 2 L.	Trunk	}	Flexion, extension, lateral adduction of trunk.
Region IV	3 L. to 2 S.	Hind limb		

Hence each of the fundamental subdivisions or parts of the body may schematically be regarded as represented in one of four regions of the cord (Region I., II., III., IV.), which may conveniently be termed the head and neck region, the fore-limb or arm region, the trunk region, and the hind-limb region respectively.

A crude classification of this sort also has the advantage of conveying reference to the physiological relationships of these parts of the body.

Historical Survey.

The general literature of the spino-cerebellar tracts is well known, but it appeared to us, in endeavouring to map out the destination of the tract-fibres, that it would be useful to tabulate the knowledge already gained as follows:—

Table A.—Historical Table of Gowers' Tract (Tractus spino-cerebellaris ventralis).

Author	Reference	Nature of Research	Abstract
Bastian ...	*Med. Chir. Trans.*, 1867, p. 499	Case of paraplegia	The tract consists of afferent fibres and is part of the dorsal or direct cerebellar tract.
Gowers ...	"Diagnosis of diseases of the spinal cord," 1879	Cases of paraplegia	Probably conducts painful sensations from the opposite side of the body; its component fibres probably arise from cells in the posterior commissure.
Singer ...	*Sitzungsb. d. K.K. Akad. d. Wissensch. Wien*, 1881, Bd. lxxxiv	Experimental degenerations	Considered tractus ventralis a spino-cerebellar one.
Testut ...	Traité d'anatomie humaine, vol. ii., p. 352	Anatomical evidence	Divides cerebellar tract into ventral and dorsal portions and states that their fibres thus directly represent long anastomoses between the superior vermis of the cerebellum and Clarke's column.
Löwenthal ...	*Revue Med. de la Suisse Romande*, 1885, p. 511.	Experimental degeneration	Lesion between fifth and sixth pairs of cervical nerves. Whole of left lateral column destroyed. Ventral portion of cerebellar tract is traced up to where it turns towards the external periphery of the superior cerebellar peduncle, and then runs backwards describing outside the peduncle a prolonged half-turn and eventually appears at the dorso-internal side of the superior cerebellar peduncle at the spot where the peduncle reaches the medullary velum of the cerebellum.

Author	Reference	Nature of Research	Abstract
Singer ..	"Ueber die Veränderungen im Rückenmark nach zeitweiler Verschliessung der Bauch Aorta," *Sitzungsb. d. K.K. Akad. d. Wissensch. Wien*, 3 Abth., 1887, 95-96	Compression of abdominal aorta Experimental degeneration	Origin of tract is in cells of anterior cornu in the lumbar enlargement.
Auerbach ...	"Zur Anatomie der aufsteigend degeneriren den Systeme des Rückenmarks," *Anat. Anzeiger*, 1890, No. 3 u. 4. Also "Zur Anatomie der Vorderseiten-strangreste," *Arch. f. Pathol. Anat. u. Physiol.* v. Virchow, Bd. 121, 1890, S. 199	Experimental degeneration	Posterior part of half spinal cord destroyed for some length. (Posterior white column, posterior horn of grey matter and posterior part of lateral column.) Degenerations in ventro-lateral cerebellar tract up to ventral part of superior vermis of cerebellum. The number of degenerated fibres in anterior and antero-lateral column decreases from below upwards.
Edinger ...	"Einiges vom Verlauf der Gefühlsbahnen im Centralen Nervensystem," *Deutsch. med. Wochenschr.*, 1890, S. 421	Anatomical work on spinal cords of fishes, reptiles and amphibia	Antero-lateral tract is probably connected with transmission of painful sensations from opposite side, but fibres come from cells of posterior horn and decussate in anterior commissure. Section of posterior roots causes no degeneration in the antero-lateral column.
Bechterew ...	*Neurol. Centralbl.*, 1890, S. 354	Myelinisation method	Gowers' tract undergoes development at a different period from the rest of the lateral column.
Mott	"Ascending Degeneration resulting from Lesions of the Spinal Cord in Monkeys," *Brain*, vol. xv, 1892, p. 215	Experimental degeneration	Antero-lateral tract divided either on one side or both sides. Ventral cerebellar tract may be completely divided in monkeys apparently without producing analgesia. Gowers' tract traced to the ventral part of the superior vermis by way of the superior cerebellar peduncle forming in its course a remarkable loop over the fifth nerve. Scattered fibres belonging to the fillet system can be traced as far as the anterior corpus quadrigeminum of the same side.

Author	Reference	Nature of Research	Abstract
Grünbaum ...	*Journ. of Physiol.*, 1894, vol. xvi, p. 368	Longitudinal division of the spinal cord	Found an ascending degeneration at the anterior border of the cerebellar tract.
		Injury to anterior cornua. Degeneration evidence	In sections above the lesion degeneration is found on both sides of the cord in the cerebellar and antero-lateral tracts.
Mott	"Experimental Enquiry upon the Afferent Tracts of the Central Nervous System of the Monkey, *Brain*, vol. xviii, 1895, p. 1	Experimental degeneration after longitudinal division of spinal cord	Unilateral section of posterior roots. Degenerated fibres sometimes found in opposite antero-lateral column. Assumes (1) These fibres come from cells of grey matter of the same side as the lesion and cross over in the anterior commissure, or (2) were damaged fibres due to vascular changes in the grey matter, the result of operation.
Pellizi	"Sur les dégénérescences secondaires dans le système nerveux central a la suite de lésions de la moelle, et de la section de racines spinales," *Arch. Ital. de Biol.*, t. xxiv, 1895, p. 89	Experimental degeneration	Ventral cerebellar tract follows course of superior cerebellar peduncle, spreads out feather-wise (*en panache*) and crossing with the fibres of the opposite side radiates into the white substance of the cerebellar folia of the anterior and inferior part of the superior vermis. Before crossing in the middle line a large bundle goes upwards to the superior portion of the superior vermis. He suggests that these fibres cross successively higher up. No fibres seen going to cerebellar nuclei. After section of posterior roots (lumbo-sacral and cervical) he observed degenerations in the cerebellar tracts!
J. Risien Russell	*Brain*, 1898, vol. xxi, p. 145	Case of tumour of spinal cord. Degeneration evidence	Gowers' tract begins at the level of the third lumbar.
Schäfer ...	*Journ. of Physiol.*, 1899, vol. xxiv, p. xxiii	Chromatolysis evidence	States some fibres of Gowers' tract arise from cells of Clarke's column.
O. Kohnstamm	*Neurol. Centralbl.*, March, 1900, S. 242	Degeneration evidence	The lesion destroyed the posterior quadrant of the cord, including the posterior horn. In Gowers' tract the more proximally arising fibres lie median to fibres arising further back.
Lubouschine ...	*Le Nevraxe*, vol. iii, 1901-2, p. 123.	Degeneration evidence	Diffuse injection lesion of posterior cornu. Concluded that the fibres of Gowers' tract arise from the posterior cornu of both sides.

Author	Reference	Nature of Research	Abstract
Collier and F. Buzzard	*Brain*, 1903, vol. xxvi, p. 559	Degeneration evidence from clinical cases	First discussed fully the relative regional origin of the spino-cerebellar tracts. Probably less than one-half of the tractus spino-cerebellaris dorsalis is cervical and thoracic in origin. Found that a mesial bundle of the tractus spino-cerebellaris dorsalis gave collaterals to the nucleus dentatus, and inferior vermis (lobes ?). The lateral main bundle also gave collaterals to the nucleus dentatus. Degenerate fibres traceable to all parts of the cerebellar cortex especially the lower part of the lateral lobe. Regard spino-vestibular fibres as of lumbo-sacral origin only. Also that Gowers' tract sends fibres to both lateral lobes and to inferior vermis, also to the dentate nucleus as well as the nucleus fastigii.
Quensel and Kohnstamm	*Neurol. Centralbl.*, 1907, S. 1138	Degeneration evidence	Regard the whole Gowers' system as arising from the posterior cornual cells of the contra-lateral side.
Schäfer and Symington	*Quain's Anat.*, 11th Ed., 1908, vol. iii., pt. 1, pp. 85, 97, &c.	Epitome of all evidence	"The dorsal and ventral spino cerebellar tracts perhaps have a common origin, possibly from the cells of Clark's column, but also from other cells in the grey matter of the same and perhaps of the opposite side."

Table B.—Historical Table of Flechsig's Tract (Tractus spino-cerebellaris dorsalis).

Flechsig ...	"Leitungsbahnen im Gehirn u. Rückenmark," Leipzig, 1876	Myelinisation evidence	The tract is derived from cells of Clarke's column. III lumbar to II thoracic segments inclusive in the dog.
Löwenthal ...	*Revue Med. de la Suisse Romande*, 1885, p. 511	Lesion between fifth and sixth pairs of cervical nerves. Whole of left lateral column destroyed	The dorsal portion of the direct cerebellar tract terminates in the restiform body. He gives reasons for connecting its fibres with the superior vermis of the cerebellum.
Auerbach ...	*Vide* reference in Table of Gowers' tract, 1890	—	Traces dorso-lateral cerebellar tract up to dorsal portion of superior vermis.
Mott	*Brain*, 1890, vol. xiii, p. 433	Degeneration evidence	The tract takes origin in the cells of Clarke's column.
	Brain, 1892, vol. xv, p. 215	Antero-lateral tract divided either on one or both sides	The dorsal cerebellar tract connects cells of Clarke's column with the dorsal portion of the superior vermis.

Author	Reference	Nature of Research	Abstract
Pellizzi ...	*Vide* reference in Table A, 1895	Degeneration evidence	Tract radiates towards the superior anterior and inferior part of the superior vermis of the opposite side decussating in the middle line with the restiform fibres of the other side. States that Mott's conclusions with regard to termination of tracts are incorrect. The majority of the cerebellar tract fibres take origin from the cells of Clarke's column; where these are not present, from groups of cells which represent them.
H. T. Patrick	*Journ. of Nerv. and Mental Dis.*, xxiii, 1896, p. 85.	Degeneration evidence	Confirms Mott.
Van Gehuchten	*Journ. de Neurol.*, Bruxelles, 1898	Chromatolysis evidence	Confirms Mott with regard to origin of tract from Clarke's column.
Schäfer ...	*Journ. of Physiol.*, xxiv, March 18, 1899, p. xxii and xxxii	Degeneration evidence	Confirms Mott.
Warrington ...	*Journ. of Physiol.*, xxiv, 1899, p. 476	Chromatolysis evidence	States also that cells are distinguished by chromatolysis and early atrophy with absence of tendency to repair characteristic of other cells.
Sherrington & Laslett	*Journ. of Physiol.*, March, 1903, p. 58	Method of "successive degeneration"	(1) Confirm Mott and Warrington. (2) Further state that the tract is stratified in the following order: Outermost—Fibres from segments furthest backward in the cord. Next — Fibres from the lowest thoracic segments. Deep to these —Fibres from thoracic segments further forwards. Innermost — Fibres from topmost thoracic and lowest cervical segments. (3) Demonstrate — That some of the fibres of the tract are long internuncial spinal fibres.
Edinger ...	"Text-book," 1890, p. 327	Anatomical investigation, &c.	The tract comes from vesicular column of Clarke, is a secondary continuation of posterior root-fibres, constitutes the main part of the spinal connection, and curving mesially enclosing the corpus dentatum, passes to the cortex of the superior vermiform process.
R. Bing ...	"Experimentelles zur Physiologie der Tractus spino-cerebellaris," *Arch. f. Physiol.*, 1906, S. 250	Physiological and degeneration evidence	After section of direct cerebellar tract in dogs found that the animals stand with abducted legs and are atactic. States that lesion of cerebellar tracts involves two primary considerations: (1) Lesion of special method of control. (2) Lowering of muscle tonus.

Author	Reference	Nature of Research	Abstract
Otto Marburg	"Die physiologische Function der Kleinhirnseitenstrangbahn," *Arch. f. Anat. u. Physiol.*, 1904, S. 457	Degeneration evidence	Shows that tractus spino-cerebellaris dorsalis has the most important share in the regulation of the "principal" movements.
Rothmann ...	*Neurol. Centralbl.*, 1907, S. 968	Degeneration evidence	Nucleus lateralis inferior, though receiving fibres from the tractus spino-cerebellaris dorsalis, receives none from the tractus spino-cerebellaris ventralis.
Münzer and Wiener	*Arch. f. experimentelle Pathol.*, 1895, Bd. 35, S. 113	Degeneration evidence	

Table C.—Other Spino-Cerebellar Tracts Described.

G. B. Pellizzi	*Vide* Table A ...	*Vide* Table A ...	*The median cerebellar tract.* To dorsal and ventral cerebellar tracts a median tract must be added equally constant although smaller. Lies between dorsal and ventral cerebellar tracts in cord and medulla, is composed of large fibres. At the emergence of N. VII its fibres tend dorsally. Then the fibres go further dorsally inwards and lie along the internal border of the ventral extremity of the ascending root of V. It thus comes into contiguity with the ventral tract, but the fibres of the two tracts are always distinct from one another. The fibres are abundant in the caudal half of the middle peduncle and lie in the internal part of its radiations. They go towards the antero-superior part of the superior vermis.
Rothmann ...	*Arch. f. Anat. u. Physiol.*, Physiologische Abtheilung, 1899, S. 120	Degeneration evidence.	*A sacro-lumbar lateral cerebellar tract* is present in dogs and lies above ventrally to dorsal cerebello-spinal tract. Many of its fibres end in the upper dorsal and cervical cord, but others pass into the medulla as a lateral cerebellar tract. Considered (p. 46) a larger part of Gowers' tract crossed the middle line of the cerebellum (1 experiment).
	Neurol. Centralbl., Nos. 1 and 2, 1900, S. 16	By embolus of cord with semen Lycopodii excluded function of conus terminalis and lumbo-sacral cord. Thus obtained degeneration of tract in posterior part of the lateral column	

From this survey of what has already been accomplished it will be seen that nothing has been yet done definitely to ascertain the relation of the spinal centres subserving the fore-limb and head and neck musculature to the cerebellar mechanism although the association of these parts is very intimate owing to the requirements of equilibration.

It appeared to us desirable to take advantage of the increased knowledge of the cell grouping in the spinal cord gained by the researches of Bruce, Parhon, and others, knowledge which has been lately supplemented by the researches of Harvey Pirie, and especially of Jacobson on the middle cell groups of the spinal cord, particularly those which occupy (1) a position in the cervical cord homologous with the cells of Clark's column, (2) the middle region of the grey cornu. From Jacobson's work, it seemed clear that although throughout the cervical spinal cord large and characteristic cells are occasionally seen in the situation of Clarke's column, the spino-cerebellar paths in the cervical regions must arise from the middle cells of the cornu.

The present research was designed and begun before the more recent normal anatomical work just referred to was published, but we had decided on grounds of homology to attempt to destroy the middle region of the cornu and therefore the "middle cells" by means of a small longitudinal lesion.

It seemed that the cells and origin of the tractus spino-cerebellaris ventralis might be regarded as lying approximately in front of a line passing through the posterior or dorsal limit of the central canal and not in the posterior cornu. It was therefore necessary to employ some means of causing the destruction of very limited areas within the boundaries of the cornu.

At the same time, in order to study separately the distribution of the cervical (*i.e.*, head and neck and fore-limb) spino-cerebellar fibres from those coming from the other regions of the cord and belonging to the trunk and hind-limb, the antero-lateral column had to be carefully preserved from injury. The injection method employed by Münzer and Wiener and subsequently by Lubouschine causes such widespread damage and is limited with so much difficulty that we did not employ it and resorted to electrolysis.

Operative Procedure and Material.

The operative procedures adopted were carried out by one of us (V. H.) as follows:

The spinal cord was exposed in the anæsthetised animal by removing the laminæ of two to three vertebræ; a minute lesion was made in the spinal cord parallel to the central canal by means of a short electrolytic needle fitted with a suitable handle and bent at a right angle. The anatomical direction given to the needle was penetration (vertically to the cord) of the posterior root zone and then headwards paralled to the central canal. The needle was made an anode, the kathode being placed on the neck muscles exposed in the wound, and electrolysis (anodal) was then performed. This in the majority of the experiments comprised the passage of a current of 1 milliampere for thirty seconds. For a larger lesion 2 ma. for one minute was employed.

The animal was kept for three weeks and then killed under chloroform after the reflex arcs and the conductivity of the cord has been tested by faradic excitation. The resultant degeneration in the brain and spinal cord was studied by the Marchi method. Excluding the cases in which the experiment failed for different reasons, we obtained complete results from one dog, two cats and eight monkeys (six *Macacus rhesus*, one *M. cynomolgus*, one *M. sinicus*).

In addition we have employed a number of sectional series of unpublished exclusion experiments in cats and monkeys made during the last eight years by one of us (V. H.), including direct and very restricted lesions of the ascending spino-cerebellar tracts and at various levels in the bulbo-spinal axis.

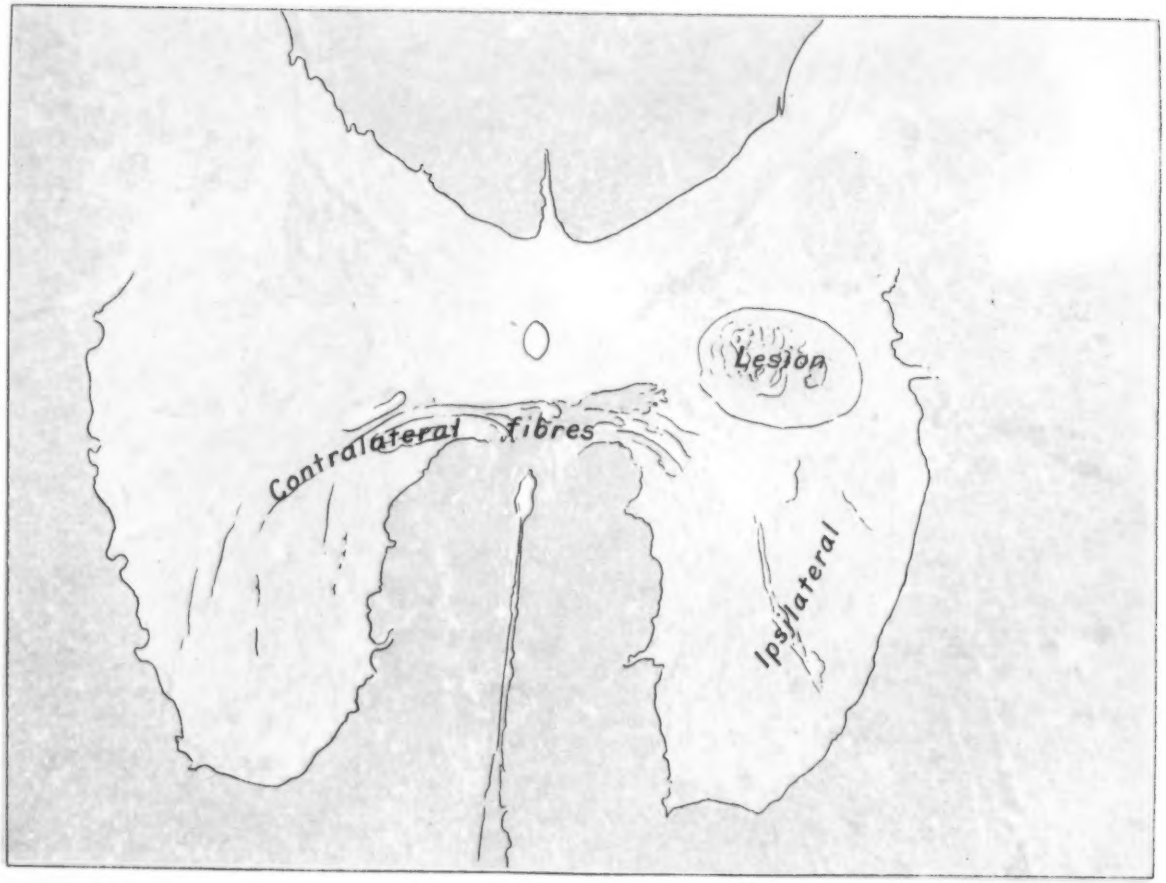
Results.

I. — *Course of Spino-cerebellar Fibres in the Various Regions of the Spinal Cord.*

Region I.

I.—*Contralateral Fibres.*

Taking the regions of the cord enumerated on p. 238, and beginning with Region I, we find that the contra-lateral fibres from cells in the dorso-medial area (Pirie's para-central and Clarke's column areas) of the grey cornu cross in the anterior commissure and through the anterior cornu to gain the contra-lateral ground bundle in which they ascend lying dorsally to the ventral spino-cerebellar tract formed by the fibres from the rest of the spinal cord.


Lesion
Contralateral fibres
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Ibérique
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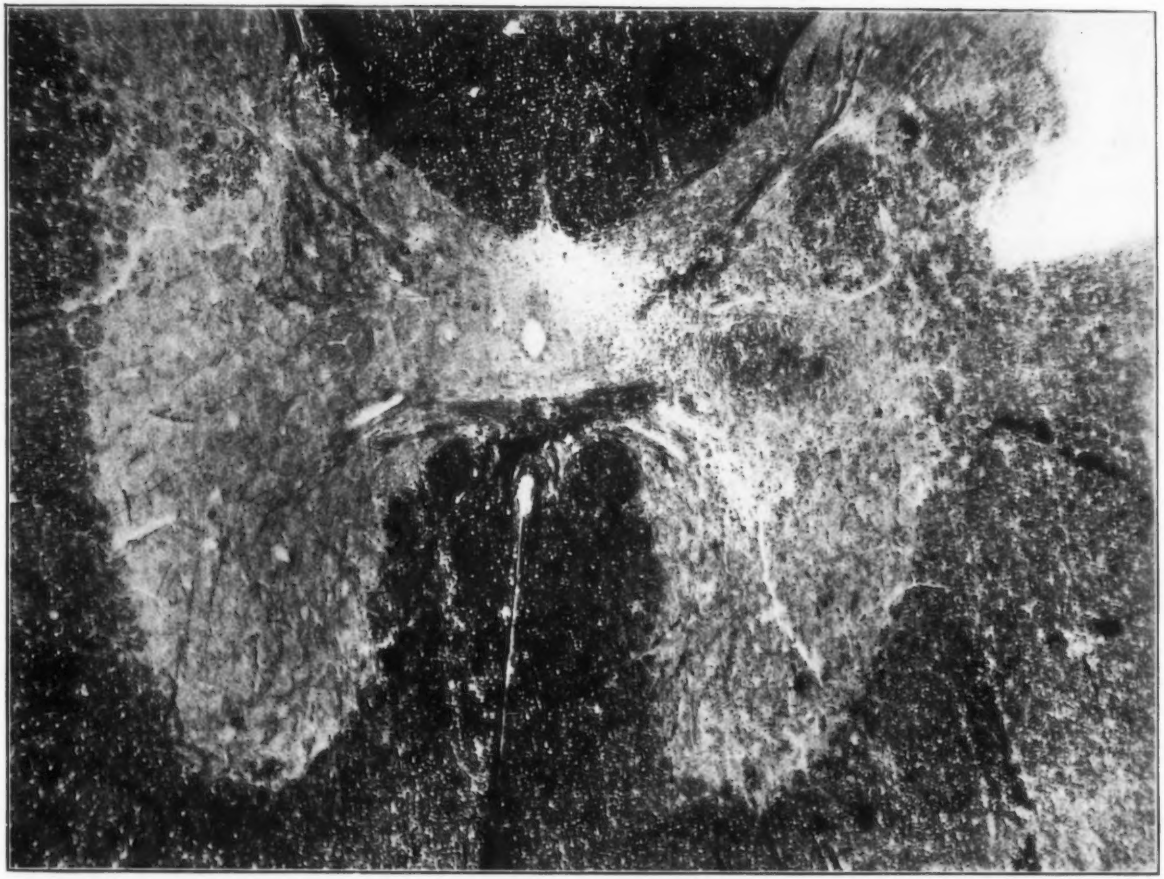


FIG. 1.

Section of the spinal cord (*Macacus rhesus* 32) at the level of the second cervical root, showing the nature and situation of the lesions employed in the present research as well as the main paths of the fibres leading therefrom.

These large fibres ascend in the pars reticularis lateralis medullæ and in *Macacus rhesus* terminate in the lobus pyramidalis of the cerebellum.

(2) The ipsilateral fibres consist of two groups, one springing from a position mesial to the intermedio-lateral area (Pirie's anterior central, central, and post-central areas) of the cornu and entering the lateral column to reach the nucleus lateralis or passing up behind the fastigio-brachial bundle near the lobus centralis and anterior part of the lobus pyramidalis. Summing up these results, therefore, it is clear that the spino-cerebellar fibres springing from the upper cervical region (head and neck movements) pass to all portions of the vermis except the most dorsal and most ventral, the parts omitted being the two anterior lobuli of the lobus posterior (Elliott Smith) and the lingula, nodulus, and uvula.

Further, these fibres, like those from lower spinal levels, give off in the medulla collaterals to the nucleus vestibularis (Deiter's), the nucleus formationis reticularis, and the nucleus lateralis.

Region II.

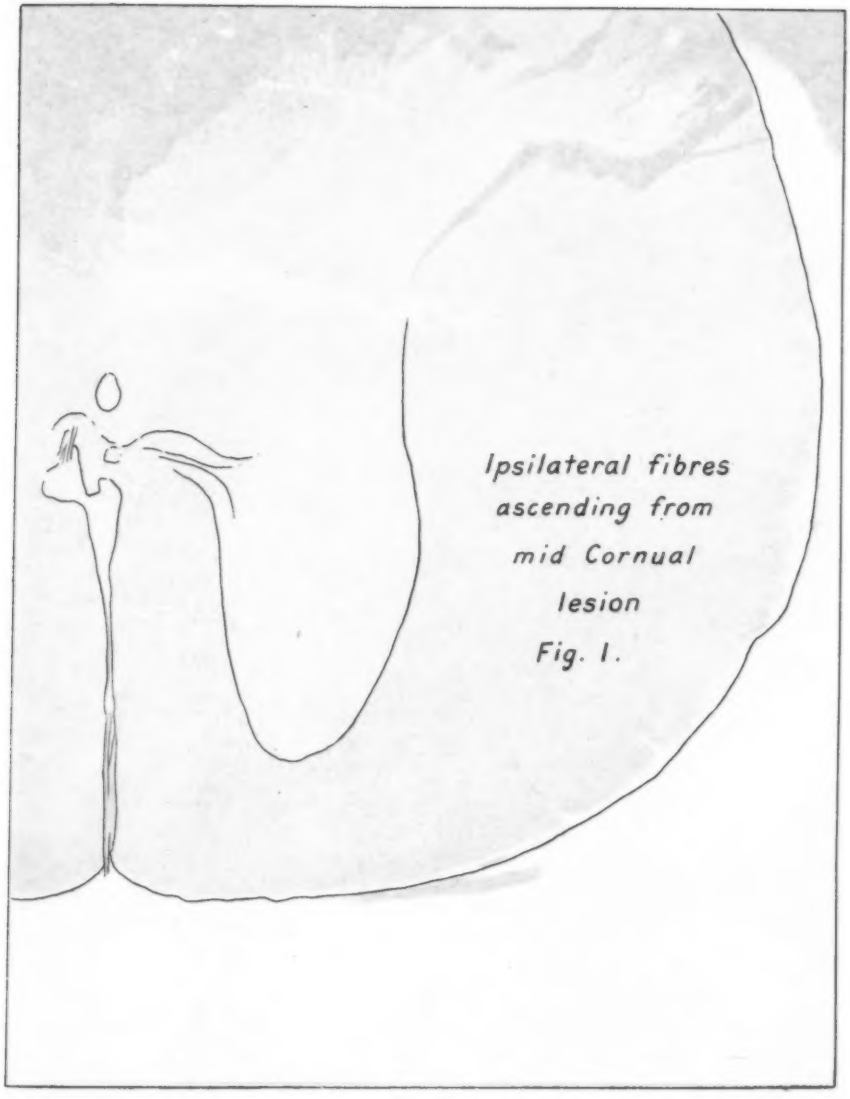
The fibres from this area of the cord are important since they constitute the spino-cerebellar tracts for the upper limb. Some of them pass to the tractus dorsalis; we may therefore commence with the the ipsilateral class.

(1) *Ipsilateral Fibres.*

Dorsal Fibres.—A few fibres pass towards the tractus spino-cerebellaris dorsalis forming the most internal group and occupying longitudinally a length of three segments in attaining their position in the area of the tract.

Dorso-ventral.—Fibres of varying diameter from the intermedio-lateral region of the cornu pass up in the lateral column at a distance from the peripheral margin of the cord to the nucleus reticularis medullæ and to the nucleus lateralis medullæ.

Ventral Fibres.—The ventrally running fibres tend to form Gowers' tract in the usual way, but they remain in the ground-bundle area of the lateral column and do not reach the surface of the cord. The most internal pass in the medulla close to the outer margin of the spinal fifth and ascend to the cerebellum lying between the fibres of Gowers' (dorso-lumbar) tract and the fastigio-brachial bundle (fasciculus fastigio-bulbaris).



Ipsilateral fibres ascending from mid Cornual lesion

Fig. 1.

Fig. 1.

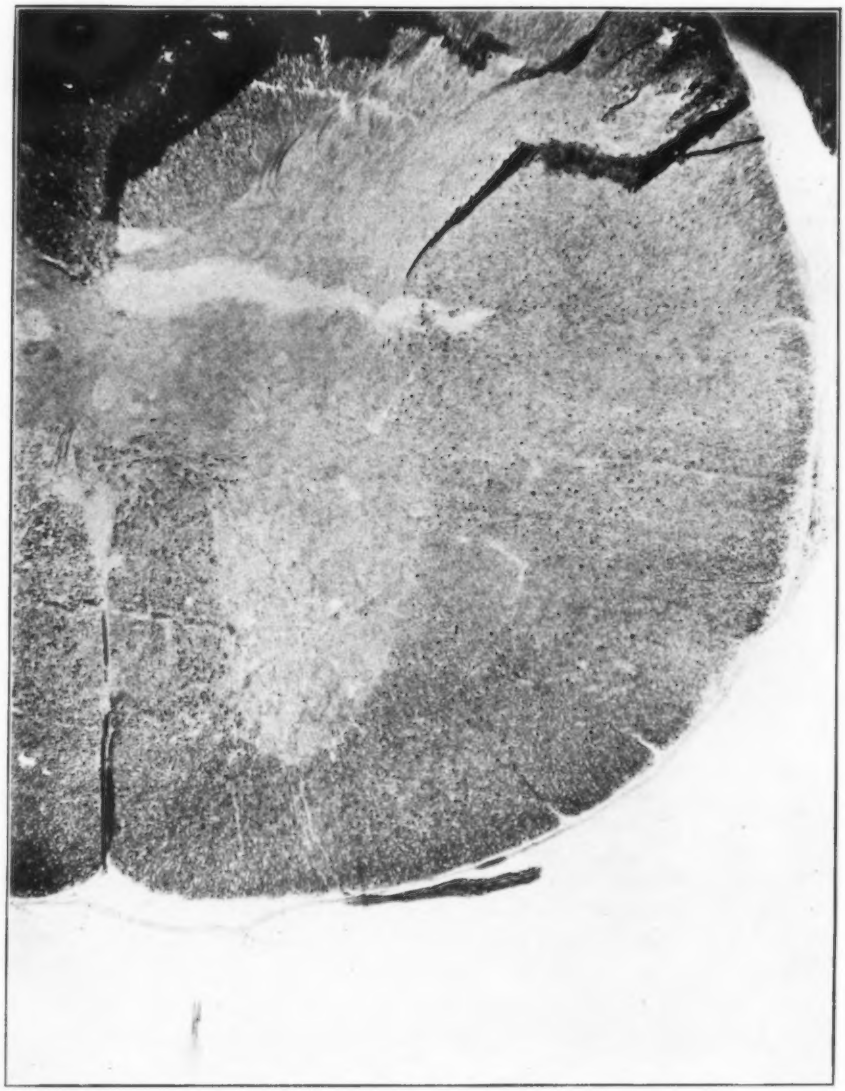


FIG. 2.

Section of the spinal cord (*Macacus rhesus* 36) at the level of the first cervical root, showing the ipsilateral fibres in the lateral column.

Thus in confirmation of Kohnstamm's observation we find that the spino-cerebellar fibres for the fore-limb occupy definitely a position dorsal, i.e., posterior to those for the trunk and lower limb but in their distribution and termination in the lobus centralis they are scattered over the whole area, and are not aggregated into any special folium. This general arrangement of the spino-cerebellar fibres in laminæ is the same as that originally pointed out by Sherrington and Laslett.

(2) *Contra-lateral Fibres.*

These are of very varying diameter and on the average smaller than those of the ipsilateral side. They run up in the ground-bundle, gradually passing outwards, and only arriving at their place in the main path after passing through about five segments of the cord. In the formatio reticularis they lie ventrally and internally to the trigeminal spinal root.

These fibres are internal to, and do not appear to send collaterals into the nucleus lateralis of the medulla. As they ascend in the formatio reticularis they gradually diminish in number.

REGIONS III AND IV.

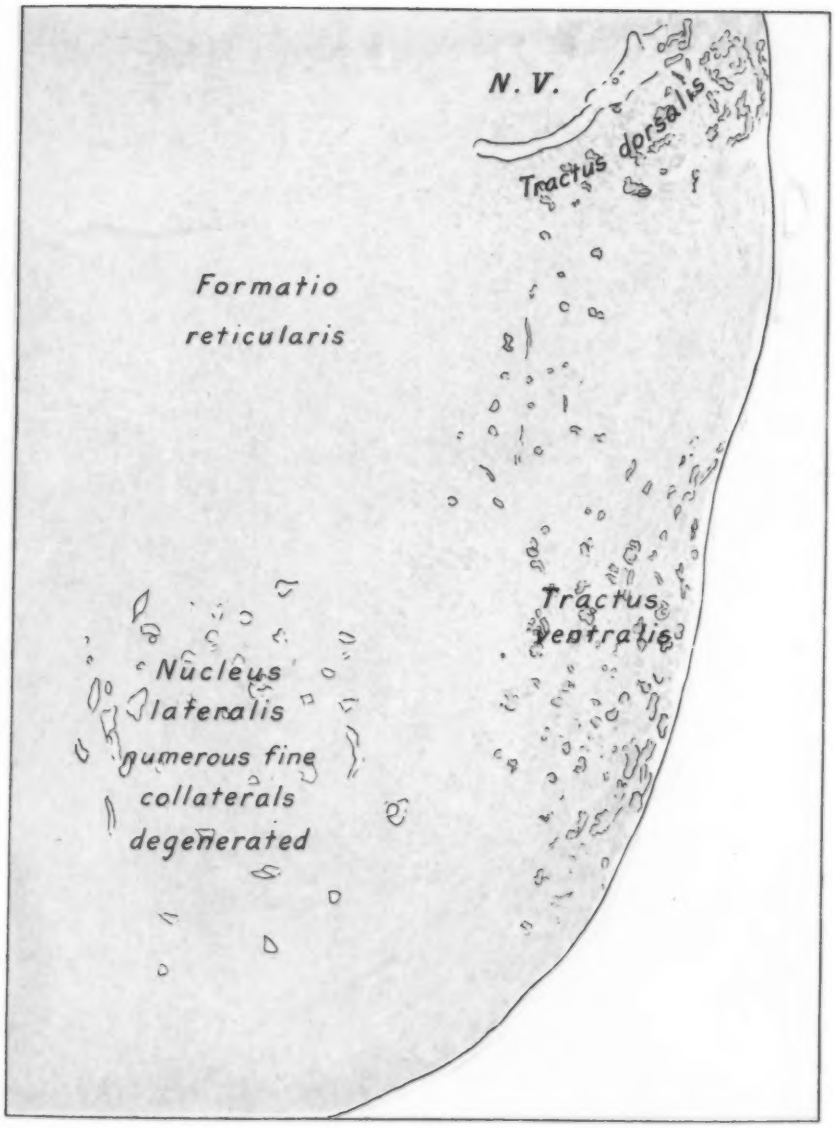
As regards these regions of the cord we have made no special experiments on Region III., and as regards Region IV., we found in control experiments that the course of the fibres in the spinal cord was as described in the text-books, and needs no repetition. The termination of the various groups of fibres in the cerebellum we will now discuss.

II.—*The Terminal Distribution in the Cerebellum of the Spino-cerebellar Tracts.*

Pellizzi, in adversely criticising the original statements of Mott relative to the termination of the spino-cerebellar paths in the cerebellar cortex appears to have fallen into the error of basing his opinions on extensive lesions of the cord only. Our experience from restricted lesions, on the contrary, confirms Mott's views, and we will now state in summarised form the results in detail.

REGION I.

The spino-cerebellar fibres of this region, which are in the main furnished through the tractus spino-cerebellaris ventralis, are distributed to the lobus centralis and culmen. None pass to the lingula.


N. V.
Tractus dorsalis
Formatio
reticularis
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ventralis
Nucleus
lateralis
numerous fine
collaterals
degenerated

N. V.
Tractus dorsalis
Formatio
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Tractus
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Nucleus
lateralis
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degenerated

FIG. 3.

Transverse section through the bulb at the centre of the nucleus lateralis from an extensive (5 segments) lesion of the mid-cornual region in the cat, showing fine collateral fibres degenerated among the cells of the nucleus lateralis.

A few are distributed to the uppermost folia of the lobus pyramidalis (*i.e.*, through the tractus spino-cerebellaris dorsalis).

Region II.

The fibres of this region, *i.e.*, arising from the fifth cervical to the first dorsal spinal segments, end in the cortex of the cerebellum as follows the lobus centralis, the ventral half of the culmen, and the ventral half of the lobus pyramidalis.

In full agreement with Mott's results we have found that the fibres of Gowers' tract (purely isolated) are practically not distributed to any part of the cerebellar cortex behind the plane of the anterior cerebellar commissure, except the collaterals which are distributed to the nucleus fastigii of the same side. Further that the distribution to the cortex is by medium-sized collaterals[1] springing from the main fibres as they cross in the anterior commissure.

These collaterals enter all the folia of the lobus centralis and ventral part of the culmen. A striking illustration of the fact that the fibres of the tractus ventralis from the hind-limb region, Region IV., of the spinal cord are distributed to exactly the same area of the cerebellar cortex as those from the fore-limb region is shown by two experiments (62 and 80, 1903, V. H.), in which extremely limited lesions of Gowers' tract were made at the first lumbar level and the third and fourth cervical level respectively. In both animals the degenerated fibres were precisely traced to the same point in the cerebellum, viz., the lobus centralis and to the ipsilateral nucleus fastigii, no fibre passing to the cortex cerebelli anywhere caudal to the posterior plane of the commissura anterior.

Region III.

We have not made any experiments on this region.

Region IV.

The termination of the spino-cerebellar fibres in the cerebellum from the caudal limb region may be limited to the discussion of the tractus spino-cerebellaris dorsalis.

According to our observations the whole tractus spino-cerebellaris dorsalis ends by freely branching fibres in the lobus centralis, the culmen, the lobus posterior, and the lobus pyramidalis on both sides of the median plane, the ipsilateral fibres being to the contralateral as 2 to 1.

[1] These collaterals subdivide very rapidly in penetrating the substantia alba of the folia.

Mott's original description is in general principle thus fully established, and it is clear that whereas the tractus ventralis is distributed principally to the folia of the lobus centralis and to a much less extent the culmen and lips of the primary fissures the tractus dorsalis not only supplies the same cerebellar cortex, but extends backwards throughout the lobus pyramidalis. Thus, the area of distribution of the tractus ventralis is anterior or headward compared to that of the tractus dorsalis.

We cannot leave this most important question without drawing attention to a reversal of the facts bearing upon it which has curiously received support so that even in the last edition of Quain's "Anatomy," vol. iii., pt. 1, 1908, p. 199, the statement is unfortunately made that "The fibres from Gowers' bundle are distributed mainly to the caudal half of the vermis on both sides."

III.—*The Connection between the Spinal Nuclei and Cerebellar Nuclei.*

(1) *Via the Tractus Spino-cerebellaris Ventralis.*

We have already discussed the supply of the tractus spino-cerebellaris ventralis to the cortex of the cerebellum. We must now discuss the precise nature of the important connection between this tract and the nucleus fastigii (roof nucleus), a connection the existence of which has been questioned. This association, which was described in man by Collier and Buzzard, is provided by numerous fibres in the rhesus and in the carnivora (cat, dog).

As the fibres of the tract cross in the anterior commissure, they send stout collaterals back between the nuclei fastigii within which finer branches of these fibres ramify throughout the whole nucleus. The spino-nuclear connection is almost wholly unilateral, few fibres entering the contralateral nucleus.

(2) *Via the Tractus Spino-cerebellaris Dorsalis.*

The dorsal spino-cerebellar tract has, so far as we can see, no connection in the cat or rhesus with the nucleus dentatus, although the fibres curve round the nucleus to reach the cortex and although such communication was observed in man by Collier and Buzzard. Absence of such connection would be, of course, in harmony with the fact that the nucleus dentatus is in relation with the cortex of the lateral lobe and therefore not, like the vermis and nucleus fastigii, in direct association with any spinal path (for the cortical relations of the nuclei, see

Clarke and Horsley, *Brain*, 1905, p. 13), but the proximity of the tracts to the fleece of the nucleus suggests an intercommunication and the point is worthy of a special reinvestigation.

The distinction between the vermis and the lateral lobes generally recognised is thus intensified.

IV.—*On the Question of the Topographical Localization of the Limbs and Part of the Body in the Cerebellum.*

From the foregoing account of the distribution of the cervico-cerebellar fibres especially those of the ventral tract, it is quite clear that by their distribution over the whole area of the vermis, which is allotted to the spino-cerebellar system, each part of the spinal cord must, practically speaking, be represented in every unit of the cortex to which the spinal fibres run. From the point of view of afferent function, therefore, there cannot be said to exist any evidence of differentiation of the cerebellar cortex into localized receiving stations for the impressions (muscular, arthric, etc.), which ascend from the arm, trunk, or leg muscles, joints, etc., respectively.

It would appear, therefore, that the cerebellar cortex is a structure in which these muscular-sense impressions are associated together, or, to use a more frequently employed expression, co-ordinated. The recent excitation and exclusion experiments by which it is believed that definite centres for the movements of different parts of the body have been demonstrated to exist in the cortex cerebelli, just as in the cortex cerebri, must, we think, be otherwise interpreted. Particularly is this the case, where exclusion experiments have been made by extirpation of parts of the cerebellar cortex, for there is no doubt that the error pointed out originally by Clarke and Horsley has not been sufficiently avoided, and that the phenomena noted have been due at least as much to lesions of the subjacent nuclei, the nucleus fastigii, dentatus, etc., and even of the nucleus vestibularis, as of the cortex cerebelli.

V.—*Symptoms Displayed by the Animals in whom Lesions of the Cervical Spino-cerebellar Tracts had been made.*

Our clinical observations on the experimented upon animals, though furnishing only few symptoms and those remarkably limited in degree owing to the very restricted character of the lesions, are, nevertheless, confirmatory of the results obtained by Marburg and by Bing.

The first notable point is the question how far interference with the spino-cerebellar tracts causes a loss of efferent (purposive) movement. No such loss was observed by us. The motor effects we observed were invariably transitory and attributable to the direct interference with the anterior cornu, or to the effects of the anæsthetic. As regards equilibration, however, and accuracy of movement in all the animals experimented upon there was to be seen ataxy and clumsiness of movement most noticeable in the upper limb. With the ataxy there was very frequently contracture and the arm of the same side was often in the sling position as described by Mott and Sherrington, after division of the (brachial) posterior roots.

On the Unilaterality of the Distribution of the Spino-cerebellar Tracts.

Several authors have noticed that the fibres of the tractus spino-cerebellaris dorsalis are distributed, more or less, to both sides of the middle line of the vermis. The bilateral distribution, both spino-cerebellar tracts, merits a quantitative consideration and the material at our disposal enables us to estimate this roughly. The tractus spino-cerebellaris dorsalis is bilaterally distributed to twice the extent of the tractus ventralis the figures being approximately

	Cerebellar distribution	
	Ipsilateral	Contralateral
Tractus dorsalis	2 ...	1
Tractus ventralis	4 ...	1

THE CONDITIONS OF FATIGUE IN THE NERVOUS SYSTEM.[1]

BY WILLIAM McDOUGALL, M.A., M.B.

OUR English word "fatigue" is a most comprehensive one. Wherever there is evidence that organic activity results in diminished capacity of the organism to carry on any of its functions, there we commonly recognize *fatigue*. Such evidence is of two kinds, objective and subjective. Of the subjective symptoms we must distinguish at least three classes :—

(1) Local sensations of fatigue, more especially in the muscles.

(2) The sense or feeling of *general tiredness*, of limpness and general incapacity for effort.

(3) The experience we call *sleepiness*.

The first of these I dismiss with a single observation You may get this sensation of local fatigue in the acutest form by holding out a limb —say, the arm—for a few minutes against the pull of gravity. After a few minutes you begin to experience in the muscles of the shoulder a disagreeable sensation, which grows rapidly more intense, until, after about five minutes, you feel that you can hardly support it. But, if you persevere, you find that there is no impossibility about doing so; the disagreeable or painful sensation grows but little more intense, if at all, after the first few minutes; you may continue to hold out your arm, and, after half an hour, there will be little more discomfort than after five minutes.

Put alongside that the fact that most good hypnotic subjects will, when in hypnosis, keep a limb held up against the force of gravity for long periods without showing any tendency to relax it, or any other symptom of fatigue.

Facts of this order seem to show clearly that such local fatigue-sensation is protective in function; that in sets it long before there is

[1] The ideas set forth in this paper were embodied in an address to the Physiological Section of the British Association at the Dublin meeting in the year 1908. That address was printed in the *Reports* of the Association, but I have sought from the editor of this journal the opportunity of bringing my ideas more prominently before the medical world by publication in these pages.

any question of exhaustion of, or serious injury to, the tissues concerned through over-action. They show that the organism has need of some protection against the possibility of self-injury through excess of activity.

And this conclusion may serve to direct our attention to the possibility of a similar function being performed by other manifestations of fatigue.

In connection with the two other classes of subjective symptoms—tiredness and sleepiness—I would draw attention to experiences of a kind that are familiar to all of us. I sit reading in the evening some difficult technical work, until, as midnight approaches, I feel thoroughly tired and sleepy, my eyes smart and will hardly keep open, my head is dull and heavy and aches a little, my whole body and my limbs feel heavy and incapable of alert movement. I then take up some thrilling story or other fascinating piece of literature; whereupon all my subjective symptoms of fatigue, both tiredness and sleepiness, disappear, and I read keenly for perhaps two hours; when I again begin to feel both tired and sleepy. Now suppose a continuation of the evening's history which is less familiar: some exciting event takes place just as I am about to go to bed—the house takes fire, or a burglar breaks in, or a friend comes in with important and interesting news that demands immediate action. Again all the symptoms of fatigue disappear, and I can perform another spell of work at high pressure, without subjective symptoms, and with little, if any, objective trace of fatigue, *i.e.*, without easily appreciable diminution of efficiency.

Facts of this order show clearly, I think, that what we commonly call fatigue, with all its diverse symptoms, objective and subjective, is no entity, that it is not due to any one kind of change in the organism; and they show that fatigue is never *absolute*, but is always *relative*. That is to say, the symptoms of fatigue are always the expression of the relation between at least two things—between, on the one hand, the work to be done, and, on the other hand, the amount of energy available at the moment for doing the work; or, in more technical language, the symptoms of fatigue are the expression of a change in the ratio between the available energy (the energy in an active living state at the moment) and the resistance which that energy has to overcome. If the task in hand is intrinsically uninteresting, the energies brought into play, liberated within the organism, or transformed from the potential to the active state, are small in quantity; therefore a small amount of work, producing a small increase of the resistances to be overcome, suffices to raise the ratio of resistances to energies above the normal, and, therefore,

to produce the symptoms of fatigue; whereas, if the circumstances are such as to bring into play greater stores of the potential energy of the organism, a much greater amount of work may be done by the organism (whether bodily or mental work), before the ratio of the resistance to the available energy rises to the point at which symptoms of fatigue appear.

Reflection upon these familiar experiences yields then two propositions which, I believe, may be two master-keys to all the problems of fatigue—at any rate, to those of fatigue of the nervous system. They may be briefly stated as follows:—

(1) Fatigue of the nervous system is a state in which the ratio of the resistances to the active energies is raised above its normal value, either through increase of the magnitude of the resistances or through diminution of the quantity of disposable energy.

(2) The function of the resistances is essentially the limitation of activity: they are thus protective of the energy of the organism; they prevent the organism exhausting its store of potential energy through unduly prolonged, intense, or widespread activity.

If these propositions are well founded we must, in order to understand fatigue, have good working conceptions on the one hand of the sources of the energies concerned and of the conditions and nature of their operations in the nervous system, and on the other hand of the nature and seat of the resistances that limit and preserve these energies.

It has recently been contended, notably by Bethe [1] in Germany and by Deschamps [2] in France, that the nervous system is not the seat of the liberation of any energy, or at any rate that such liberation is no part of its specific functions, but that it merely distributes the active energies supplied to it by *stimuli* of all kinds and by the various organs of the body. I think most physiologists will hold that this view is quite unacceptable, and that the activity of the central nervous system does essentially and always involve liberation of energy, transformation of energy from the potential to the active form, and a consumption or using up of stores of potential energy. Verworn [9], who has made himself the protagonist of this latter view, seems to me to have proved it by his own experiments and those of his pupils, although, even without these particular experimental results, there was hardly room for doubt about the matter. Further, Verworn's experiments on the spinal cords of frogs confirm the view (about which also there was little room for doubt apart from these experiments) that fatigue may be produced by either of two processes, and that it commonly is produced

by their conjunction—namely, (1) the process of accumulation of waste products of metabolism, CO_2, lactic acid and other substances; (2) the using up of stores of potential energy through excess of katabolism over anabolism. The former is called by the Germans "Ermüdung," the latter "Erschöpfung," and some English writers have proposed to use the words fatigue and exhaustion in these two senses, as the equivalents of these German words. I do not think we can profitably specialise these words in this way;[1] but, if not, we must have new words, for there can be little doubt that both processes take part in the production of fatigue, and we must distinguish between them and hold fast the two conceptions.

The question then arises—What are the seats within the nervous system of these two processes, "Erschöpfung" and "Ermüdung"? Verworn's view may perhaps claim the adherence of a larger number of physiologists than any other. It is very simple. According to this view, the cell-bodies or "ganglion cells" are the seats, or at least the principal seats, of both processes; and of both processes the essential result, which determines all the symptoms of fatigue, is a diminished katabolism and output of energy by the cell-bodies affected. "Erschöpfung" is thus, according to this view, a strictly local process, affecting only the bodies of the nerve-cells involved in any activity; while "Ermüdung" is both local and general, because the cell-body is liable to be poisoned not only by the waste products of its own activity, but also by those of the metabolism of other nerve-cells and of other tissues of all parts of the body, especially the muscular tissues; for these waste products, wherever formed, may pass into the blood and lymph and so may reach the "ganglion cells."

Now I venture to say that this picture of the nature of fatigue of the nervous system is very much too simple; the conceptions are, I contend, true and useful, but inadequate to the explanation of the complex manifestations of fatigue which meet us as soon as we consider the organism as a whole; and they are inadequate also for the explanation of many of the special and local manifestations of fatigue.

The picture needs, it seems to me, to be complicated by two most important additions. First, Verworn's scheme takes little or no account of the resistances that the nervous energies have to overcome. Now, if with him we regard the cells as seats of explosive decompositions, and

[1] Because we need the word "fatigue" to denote the state of diminished efficiency of the organism as a whole commonly produced by these two processes in conjunction, and we need the word "exhaustion" to denote the extreme degree of the state resulting from excess of katabolism over anabolism.

the nerve-fibres as freely conducting excitations (either purely physical processes or, with more probability, as physico-chemical processes involving metabolic changes similar to those that occur in the cell bodies), then it is obvious that there must be points or parts of the nervous tracts which delimit functional units and groups of units; else, instead of the orderly sequence of nervous excitations, which normally results from any stimulation, the excitation would spread indefinitely throughout the nervous system, soon producing incoördinate general activity and a rapidly ensuing general exhaustion; in the way the results of which we see in the convulsions of strychnine poisoning.

Now the question, Where, in what structures, do these *resistances* reside? is one of secondary importance perhaps, so long as we recognize their nature and function. Still it is a question of some interest. In a recent paper Verworn recognizes the existence of resistances, and assigns them, like all the other peculiarities of the central nervous system, to the cell-bodies [10]. To that view serious objections may be raised. To mention only one, it is difficult to suppose that the cell-bodies are the seats both of explosive decompositions that liberate energy and also of the resistances that delimit the paths by which the excitation spreads towards the efferent nerves. On the other hand, there are many considerations tending to show that the principal seats of these resistances may be the synapses or places of junction of the neurones.[1]

If we assume that the synapses are the seats of the resistances, and that the process of transmission of the impulse across the synapse is one that results in a temporary raising of the resistance of the synapse, then we have a conception which enables us to account satisfactorily for many manifestations of fatigue. I will point out a few of the facts

[1] See especially Sherrington's "Integrative Action of the Nervous System," Lecture I. In spite of all that has been written of the synapse in recent years, one still finds widely accepted the following argument: The nervous system consists of cell-bodies and nerve-fibres, therefore all those of its properties that are not displayed by peripheral nerves are due to the cell-bodies. Verworn himself still uses this argument, and so little is the conception of the synapse understood that Verworn, in a recent paper, interprets Sherrington as meaning by the term "synapse" the place of junction of the axis cylinder and the cell-body of a single neurone. That, I take it, is implied when he writes, "Goldscheider und Sherrington denken an die Uebergangstelle des Nerven in den Ganglionzellkörper, an die 'Synapse,' wie Sherrington sich ausdrückt" (*Op. cit.*, p. 134). Sherrington inclines to the view that the process of transmission of the excitation across the synapse is a purely physical one (*Op. cit.*, p. 17); but if, as he also inclines to believe, it is a process very readily affected by the presence of toxic substances in the blood, and if it has the effect of immediately and temporarily raising the synaptic resistance (fatigue), and of ultimately leaving it (when the fatigue effect has passed away) permanently diminished (habit), these effects would seem to demand for their explanation the assumption of some metabolic activity at the synapse. In a paper in *Brain* (vol. xxiv.) I have adduced other arguments in support of the assumption of intercellular substances, the seats of synaptic metabolism of a highly specialized kind.

which seem to point to the synapse rather than to the cell-bodies as the principal seats of the increased resistance. It has long been notorious that nerve-fibres are but little, if at all, liable to fatigue; and there is good reason to believe that the cell-bodies also are fatigued, not easily or rapidly, but only under prolonged activity or when deprived of the normal means of recuperation—deprived, that is, of the normal blood-supply. Yet we have evidence that local fatigue may be rapidly induced, and may as rapidly pass away, in the various levels of the nervous system.

Such local fatigue occurs in the reflex arcs of the spinal cord, if a stimulus is continuously applied to the afferent path [8]. It occurs in the motor region of the cerebral cortex if one spot be continuously or repeatedly stimulated [4]. It occurs still more readily in the higher levels of the brain concerned in perception—*e.g.*, in all the cases of ambiguous figures which may be perceptually interpreted in two or more different ways, and of which the different modes thrust themselves alternately upon consciousness. I have studied these alternations and shown reason to suppose that a rapidly induced local fatigue of the higher cortical paths concerned is the principal condition of this alternating activity [5]. In the same way the extreme liability to fatigue of the paths of the higher cortical levels seems to underlie the extreme instability of all our thought processes; the fact that our attention can never be held fixedly and unchangingly upon any single feature of an object, but always, in spite of all voluntary efforts to the contrary, passes on from feature to feature, or plays to and fro over the object of thought.

In all these cases we seem to be dealing with a rise of the resistance of a nervous path rapidly induced by its activity and as rapidly passing away; a rise of resistance which serves to divert the excitation-process from the path to some other channel, and so to prevent the injurious effects of a too-prolonged activity of any one path.

These are manifestations of local fatigue, of increase of the ratio of resistance to energy, induced not by diminution of energy, but by increase of strictly local resistance.

Again, experiments with the ergograph have been used much in the study of fatigue, but one interesting feature of such experiments has been unduly neglected, I think. I draw attention to it in this connection, because it seems to bear out the view I am setting forth.

The subject of the experiment has to lift a heavy weight repeatedly at brief intervals, by bending as far as he can his middle finger. Fatigue very soon manifests itself in the form of a diminished extent of the bendings

of the finger. Now, if you carefully observe the subject as he continues to repeat his efforts, you will usually see that, while at first he contracts only the muscles immediately concerned in the flexion of the finger, other muscles come into play as the flexions become diminished in extent; first the muscles of the upper arm, then those of the shoulder, then those of the trunk, still later the muscles of the lower limbs and of the arm and shoulder of the opposite side, and even those of the face, jaw, and neck on both sides. There takes place, in short, a spread or march of the excitation (not unlike the march of Jacksonian epilepsy) from the motor tract directly concerned in producing the flexion of the finger to adjacent motor tracts, then to successively more distant tracts.

Now this is just what must occur if, while the supply of liberated nervous energy is maintained at a high level of potential, and while the subject continues to direct it towards the one set of muscles, the resistances of the paths through which the excitation reaches those muscles are liable to be rapidly raised owing to the intensity of the process and to its repetition at brief intervals. The excitation will overflow, first into the most nearly connected tracts; later into those successively more remote, as the resistances of the more nearly connected tracts become in turn increased.

A very brief rest suffices to abolish or to diminish in very large degree any fatigue symptoms induced by ergographic work; and if in the ergographic experiments the intervals between successive bendings of the finger are made equal to several seconds, the evidences of fatigue are much diminished.

We have then abundant evidence of the rapid production of local increase of resistance in the central nervous system, and all that we know of the cell-bodies and of the axis cylinders makes it improbable that they can be the seats of these rapidly induced and very transitory local increases of resistance. Further, the fact that these local increases of resistance seem to be most rapidly induced in the higher levels of the central nervous system, where the connections between neurones must be regarded as least intimate and fixed, and to be least rapidly induced in the reflex arcs of the spinal cord, where the connections between afferent and efferent neurones are most firmly established, is in harmony with the view I am defending, and seems unintelligible if the alternative view is adopted.

It seems probable that the resistance of the synapses is liable to be temporarily increased not only locally by the transmission of the nervous

excitation across them, but also generally by the influence of the waste products of metabolism brought to them in the blood, for they seem to be easily affected by chemical influences of many kinds.[1]

If so, then such action of waste products upon them must play a large part in that general increase of the ratio of resistance to energy which constitutes general fatigue, and which manifests itself subjectively in general tiredness and in sleepiness; and also in the onset of sleep or general quiescence of the brain, the most important of the modes in which the organism protects itself against exhaustion.

If we provisionally accept this view, that the synapses are the principal seats of resistance, and that their resistances are liable to be thus increased both locally and generally, then the simple picture of fatigue which I have associated with the name of Verworn becomes considerably complicated. In addition to local "Erschöpfung" of the neurones, and to local and general "Ermüdung" of them by waste products, the former of which means local, and the latter both local and general, diminution of energy supply, we recognise both local and general increase of synaptic resistances. We have then, I think, a scheme much less inadequate to the explanation of those familiar and important peculiarities of fatigue to which attention was drawn in the opening paragraphs.

But there were, I said, two complications to be added to the simple Verworn picture. We have added the resistances varying from local and from general causes. The second complication concerns the sources of the energies involved in bodily and mental activity.

According to the Verworn scheme every cell-body is, I take it, to be conceived as capable of generating or transforming or liberating a certain quantity of energy, which, up to a certain upper limit, varies with the intensity of the stimulus applied to the cell; and this energy is to be regarded as finding its field of operation wholly within the neurone or the particular small functional group of neurones within which it is liberated; and all neurones are of appreciably equal value in this respect.

But there is another conception of the mode of operation of nervous energy which goes back at least as far as Descartes; the conception—namely, that the energy liberated by chemical change, by katabolic process, in one part of the nervous system may be conducted through the nervous channels and may operate in other parts of the nervous system. This may be called *the hypothesis of the vicarious usage of*

[1] There is something to be said for the view that they are the seats of the primary and principal influence of various drugs, possibly of alcohol, chloroform, strychnine, and others.

nervous energy. Now it seems impossible to get the physiologists of the laboratory, the physiologists who are chiefly concerned with the organs rather than with the organism, to consider this conception seriously and on its merits. If they occasionally refer to it, it is only to put it aside contemptuously as a naïve survival from the dark ages. Yet those who are in the habit of dealing with the problems of the organism as a whole, the physician and the psychologist, constantly make use of this conception, for they find it impossible to make progress in the understanding of their problems without it.[1] That fact gives the conception a claim to a more serious consideration than it has commonly received from the physiologists.

The conception towards which the study of the organism as a whole points is that the neurones of the afferent side of the nervous system (including the cerebellum) constitute a great common reservoir of free energy, in which the head of pressure varies from moment to moment with the ratio of the in-flow to the out-flow, and on which all efferent paths may draw in turn when they come into activity.

As to the sources from which this reservoir of free energy is supplied, no doubt every one of its constituent neurones is capable of making its contribution, and especially all those directly connected with, and stimulated through, the sense-organs.

But we shall never understand the problems of fatigue, or any other of the great problems of the brain, until we adequately recognise certain special sources of supply. And the study of fatigue serves to bring into prominence the importance of these special sources of energy.

In psychology we speak of instincts or innate dispositions to action, and we recognise that the constitution of every human being comprises a certain number of such instinctive dispositions, and that, when any one of these is awakened, whether by sense-impression or idea, the subject experiences a state of emotional excitement, and an impulse, a desire or aversion, a strong conation or felt tendency towards some kind of action. We recognise that under the driving power of such an impulse the subject can achieve tasks, can put forth quantities of energy, such as are impossible for him in the absence of any such conative-affective excitement.[2]

[1] The necessity of conceiving nervous energy in this way was urged as long ago as 1886 by Hale White (*Lancet*, vol. ii., 1886, p. 161; see also *Brit. Med. Journ.*, October 17, 1908), who proposed to use the word "neurorrheuma" to denote nervous energy so conceived. Among many others who have approved of this conception are Victor Horsley (Hughlings Jackson Lecture, *Brain*, vol. xxix., p. 448), and S. G. Sharkey (Presidential Address to the Neurological Society, *Brain*, vol. xxvii., p. 12).

[2] For a fuller discussion of the *rôle* of these innate dispositions in the maintenance of human activities, I may refer to my *Introduction to Social Pyschology*.

It is for the physiologist to discover, if possible, the neural seats and bases of these innate dispositions. Recent work by Pagano seems to indicate that they may perhaps be found in the basal ganglia of the brain [6].

But however that may be, it seems safe to assume that these powerful impulses, which we experience in conjunction with our emotional excitements, and which enable us to energise in a way quite impossible in their absence, have nervous correlates, and that the physiological correlate of such an impulse is a great liberation of energy, in some centre or part of the central nervous system, which energy augmenting greatly the disposable free energy of the brain, can be utilised in the performance of any kind of action undertaken for securing the satisfaction of the impulse: and it seems that such an accession of energy can overcome the increased resistances obtaining in a state of moderate general fatigue, abolishing more or less completely in so doing both the objective and the subjective symptoms of fatigue; because the great accession of energy lowers the ratio of resistance to energy.

It is the possibility of these sudden accessions of energy that has rendered wellnigh futile all the many attempts hitherto made to obtain reliable objective measures of degrees of fatigue of the organism as a whole.[1] Rivers [7] has recently shown how great a disturbing factor in ergographic work is "interest," and the awakening of interest on the part of the subject means essentially the bringing into play of one or more of these special sources of energy.

Again, in such fatigue experiments as those of the Kraepelin school, the fatigue effects are constantly complicated, obscured, and rendered doubtful by variations of interest or of impulse which show themselves in spurts of all sorts.[2]

It is only when we take into account these special sources of energy that we can begin to understand the way in which, under circumstances that powerfully evoke our native impulses, we can execute without

[1] Binet and Henri have shown the inadequacy of the various methods employed previous to the date of publication of their work—*La Fatigue Intellectuelle* (1898); and in a recent critical study of the principal methods Ellis and Shipe (*American Journ. of Psychology*) have arrived at the conclusion that none of those investigated by them are reliable.

[2] The Kraepelin methods, I may remark in passing, seek to avoid these disturbances by keeping interest at a minimum. But the human subject is not easily kept in such a state, he will become interested, if only in the approaching end of his task, and hence great irregularities. In view of these difficulties I have suggested a method of estimating fatigue, which follows the opposite principle and seeks to keep interest at a maximum throughout, the task set being of the nature of a sprint; and I venture to think that this is the sounder and more hopeful principle to follow: see "A New Method for the Study of Concurrent Mental Operations and of Mental Fatigue" (*British Journal of Psychology*, vol. i.).

fatigue tasks which in less favourable circumstances would render us prostrate with every symptom of fatigue.

James, in a recent lecture entitled the "Energies of Men" [3], has dealt, in his brilliant way, with this aspect of our problem; he brought forward many examples of the way in which, under conditions suited to bring their powers most fully into play and to sustain their interest at a maximum, men may achieve incredibly severe and sustained efforts. He quoted especially the case of Colonel Baird Smith, who conducted the siege operations before Delhi during the Sepoy Mutiny, showing how for months he hardly ate or slept, or rested in any way, but worked almost continuously at tremendous pressure without showing or feeling fatigue, and how then, when the end came, and the circumstances ceased to demand and excite his efforts, he collapsed, an inert, emaciated, almost lifeless invalid.

Such cases illustrate again my main points—namely, (1) that fatigue is protective; (2) that fatigue is relative, is the expression of a rise of the ratio between resistances and energies; and they show how, if the conditions are such as effectively to call into play all the great special sources of energy, this ratio may be kept from rising above the normal, until the whole organism approaches absolute exhaustion; whereas, on the other hand, under conditions of boredom, the ratio is very readily raised above the normal.

If, then, there is any truth in what I have said of these sources of energy and of the vicarious usage of energy, it follows that we have to recognize as a second condition of general fatigue, in addition to the presence of products of metabolism in the blood, a diminution of the disposable energy, due to a diminished metabolism of the neurones in general and of these special sources of energy in particular; and the possibility of general fatigue of this nature is, I think, especially important from the point of view of the physician.

The long continuance of the chronic fatigues with which the physician so often has to deal seems to show that, in many cases at least, these are not toxic fatigues (the only kind of general fatigue admissible under the too simple Verworn scheme). It seems to imply the exhaustion of some of the sources of energy, which, rendering the maintenance of a due general pressure or potential of free energy impossible, causes the ratio of resistance to energy in all parts of the nervous system to remain at a high level.

In conclusion I would suggest that the conception of fatigue as an increased ratio of resistance to energy may possibly help us in arriving at an understanding of some nervous disorders.

A due balance between resistances and energies is essential to health, and it seems possible *a priori* that the balance may be disturbed by disorder primarily affecting either factor.

Suppose that, as an innate constitutional peculiarity, the resistances are deficient relatively to the energies in an otherwise normal or well-endowed brain; we should expect to see the possessor of such a brain an excitable sensitive person who, the great protective system being deficient, easily works himself to the point of exhaustion; exhaustion rather than fatigue will be his peculiarity. He is readily provoked to a great and rapid output of energy, and his brain does not easily return to rest; general excitement is slow to die away, and he finds difficulty in sleeping after any effort, for the condition of increased and predominant resistance throughout the brain is not easily attained; the system remains uselessly at work and wears itself out: there follows exhaustion secondarily developed, owing to the deficiency of the protective system of resistances. We should then get the typical picture of the hereditary or born neurasthenic; the disorder is brought on by any strenuous course of life, and its early stages are characterized by hyperæsthesias of all sorts, undue sensitiveness to all sense-impressions, general irritability or irritable weakness, insomnia, increased reflexes; the patient may have the power of working extremely effectively for a short time, but such work soon leads to exhaustion and leaves the patient incapable for a long time of again getting up a sufficient head of nervous pressure to renew his labours. It is, I think, in harmony with this view that some of our most brilliant and original intellects have shown marked neurasthenic tendency, *e.g.*, Charles Darwin and Herbert Spencer.

The neurasthenia induced by shocks—*e.g.*, the mental and physical shocks of a railway accident—may possibly be brought into line by the supposition that the brief and general over-stimulation of the nervous system, which was too sudden to allow the increase of resistances to play its normal protective part, has more or less paralysed the synapses, so that they no longer are capable of building up and maintaining the due resistances; and again irritable weakness dominates the scene.

In this way it seems to me we may perhaps account for the paradoxical character of neurasthenia, for its combination of excess and defect of energy, the difficulty of getting up steam, the easy and rapid running down of the effort, if an effort is successfully initiated.

There is another great type of functional disease—*hysteria*, so like and yet so different from *neurasthenia*, which seems to be also a form of chronic fatigue.

Here possibly the primary evil is a constitutional defect of the energies relatively to the normal resistances. Such relative defect is apt to be brought to light by any course of life that makes considerable demands on the nervous energies, and shows itself in the failure to maintain the unitary functioning of all the many neural systems and sub-systems that make up the brain. The systems tend to become functionally separated from one another, because the supply of energy is insufficient to overcome the resistances of the highest levels of the brain and to keep open the connecting channels; hence each neural system tends to function independently of the rest, and each, being removed from the reciprocal control and inhibition normally exerted by all the rest, may function in excess, or, on the other hand, may lie dormant. Hence we get the curious pictures of overactions combined with partial defects of action, of hyperæsthesia with anæsthesia, of local contracture and paralysis, of incapacity for effort and violent convulsions, of fixed ideas and of easily changed convictions, of extreme suggestibility and extreme obstinacy. We get the characteristic symptoms of mental dissociation,[1] and in extreme cases we get the falling asunder of the neural basis of unitary personality into two or more functional systems, each of which becomes more or less fixed in its isolation; and we thus get the most strange of all the functional disorders—the cases of divided or multiple personality.

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THE PATHOLOGICAL EXAMINATION OF TWO CASES OF AMYOTONIA CONGENITA WITH THE CLINICAL DESCRIPTION OF A FRESH CASE.

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THE object of this paper is to place the pathological nature of the malady, first described by Oppenheim in 1900, upon a firm basis, and to emphasize certain clinical features of the disease which are peculiar and which, in our opinion, demand the recognition of the condition as a separate clinical entity, not to be included among the hitherto described maladies which are rightly grouped together under the term myopathy. Since Oppenheim first described the disease in 1900, though many cases have been recorded from the clinical side, there have been but three pathological examinations, and of these three only one can be said to have been complete. Spiller in 1905 was the first to make a pathological investigation upon a well-marked case at the age of 22 months. He found no changes in the nervous system, but a condition of intense regression in the affected muscles, and, in addition, a pathological state of the thymus gland. Bing in 1907 removed a portion of muscle from a patient aged $3\frac{1}{2}$, and the changes that he found were comparatively trifling. Baudouin in 1907 made a complete and detailed examination of a patient aged 4 months. He found intense regressive changes and sclerosis in the affected muscles, and he was the first to point out the greatly hypertrophied muscle fibres which were seemingly not present in Spiller's case. Further, he found conspicuous changes in the nervous system, which comprised certain changes in the external group of the ventral horn cells, smallness of the ventral roots suggesting

arrest of development and a corresponding abnormality in some fibres of the peripheral nerve-trunks. Sclerosis of the thyroid and of the thymus gland were present. Baudouin came to the conclusion that the sum of the anatomical changes was just such as is met with in cases of myopathy.

The results of our investigations upon the two cases here reported closely resemble the findings of Baudouin, and since the difference between the findings in Spiller's case and in Baudouin's case was a difference of degree rather than of kind, we may say that the four pathological investigations now on record are mutually confirmatory, with the one exception that the striking changes found in the thymus by Spiller, and in the thyroid and thymus by Baudouin, were certainly not present in one of our cases, and there was no clinical evidence of their presence in the other case. We suggest, therefore, that the changes in these glands were fortuitous, and that such changes play no part in the essential pathology of the disease.

In the interpretation of the pathological findings the exceedingly difficult problem arises as to the relative parts played by (1) arrest of development, (2) regression, and (3) regeneration, in the production of the histological changes. The fact that the investigations have been carried out upon subjects at widely different ages—namely, at 4 months, 22 months, 3 years and 7 years respectively, all these cases being congenital and not differing widely in the depth of the affection—suggests that the nature of the changes found at the different ages when the disease had been present for increasing periods would throw some light upon this question. As a matter of fact, however, the differences between the changes found at the various ages prevents us from coming to any conclusion upon this matter. For Baudouin's patient, who was only 4 months old, presented the most conspicuous changes of all the four cases; while in Spiller's clinically severe case, aged 22 months, the changes were the least marked; while the changes in our two cases, aged 3 years and 7 years respectively, were not more intense in the younger child, though clinically the younger child was far more severely affected than the elder. The objective pathological evidence seems in favour of increasing regressive changes without any regeneration; the clinical evidence suggests a developmental error in that the malady is almost always present at the time of birth, and it demands a pathology that admits of improvement, for not only is the history of progressive improvement common in the history of the recorded cases, but also the subsequent history of two of the cases that were pub-

lished by one of us (James Collier) with Dr. Wilson in *Brain*, vol. xxxi, 1908, puts the question of recovery beyond doubt. In the first of these cases, a severe congenital case which had been under the close observation of Dr. Whait from the time of birth, slowly progressive improvement occurred up to the seventh year when the knee-jerks were obtained for the first time. After this more rapid improvement occurred, and the boy can now walk fairly well at the age of 9 years. In the second case complete recovery of the upper extremities, which were severely affected, has occurred with return of the deep reflexes in the upper extremities, while the lower extremities have improved greatly. At the same time we must point out that two cases which have come under our notice have shown progressive deterioration, and one of these is the case here reported. Our interpretation of our pathological findings allows of the possibility of improvement, but it argues forcibly for the occurrence of progressive deterioration in some of the cases.

The similarity of the morbid anatomy of amyotonia to that of the myopathies is certain, and does not admit of any discussion; but the clinical aspect of this disease is so widely different from that of any hitherto described form of myopathy as to warrant, in our opinion, the retention of a separate name for this distinct clinical entity. Although more than forty cases of amyotonia have been recorded, yet until quite recently no case had been brought forward in which there was any hereditary or familial tendency, or in which a familial association with myopathy had occurred. Sylvestri, however, has recently recorded two cases of undoubted amyotonia in which all these associations were manifest. These patients were the first and fifth children of a goitrous mother, the second and third children were healthy, and the fourth was a cretin. A maternal aunt suffered with the Landouzy-Dejerine form of myopathy. The elder of the two children presented well-marked amyotonia from the time of birth, and she progressively improved till the age of 16 years. During these years her condition had changed from one of "absolute flaccid paraplegia with paresis of the upper limbs" to one of "a certain degree of general asthenia." It is somewhat difficult to follow Sylvestri in his further description of this case, for he says that at the age of 16 years, "so far as could be judged by sight, she presented the most typical picture of Erb's disease, complicated with a form of progressive muscular dystrophy (juvenile form of Erb). The left deltoid, supraspinatus and triceps were hypertrophied, and the right brachialis anticus was pseudo-hypertrophied."

In the younger child the amyotonia was typical, all the voluntary muscles being severely affected with the exception of those supplied by the bulb. In neither of the cases was there any pathological examination. The familial incidence of these cases and their hereditary and familial association with myopathy do not controvert the fact that in all other recorded cases these associations have been absent. We do not think, therefore, that it is justifiable in the present state of our knowledge of this malady to depart from the opinion that one of the characteristic features of amyotonia is the absence of hereditary and familial tendencies and of associations with myopathy. This has been the opinion of nearly all writers upon this subject, and with it our own clinical experience of the disease is in accord.

We wish to emphasize in this place those clinical features of amyotonia which are widely different from those occurring in any form of myopathy. These are as follows:—

(1) The absence of any familial tendency in the incidence of the disease.

(2) The absence of any familial or etiological relation with myopathy.

(3) Amyotonia is in the majority of cases congenital. In a small minority of cases it appears suddenly and in fully developed form after certain acute diseases.

(4) The local wasting and weakness of an individual muscle, or of a group of muscles, that are characteristic of all forms of myopathy are not met with in amyotonia.

(5) Affection of the periphery of the limbs, and especially of the intrinsic hand muscles, which is the invariable rule in amyotonia, is of the greatest rarity in any form of myopathy.

(6) Amyotonia never spreads to regions previously unaffected. Slow spreading of the affection from muscle to muscle is a characteristic of all forms of myopathy.

(7) The deep reflexes are absent from the first in amyotonia. In myopathy they are present at first, and they slowly diminish and are lost as the affection of the muscles concerned increases.

(8) The deep reflexes may appear in amyotonia when improvement occurs and, having appeared, remain permanently. In myopathy the deep reflexes never reappear after disappearance.

(9) A majority of the recorded cases of amyotonia have shown a tendency to improve progressively, and this improvement may reach a stage of practical recovery.

Our best thanks are here expressed to Dr. Ormerod, under whose

care one of the patients here reported was admitted into St. Bartholomew's Hospital suffering with a pneumonia which proved fatal; and to Dr. Langdon Brown for his kindness in providing us with the pathological material.

Clinical Details.

Case 1. (This case has already been recorded upon the clinical side by one of us [J. C.] with Dr. Wilson in *Brain*, vol. xxxi., 1908.)—S. A. I., a boy aged 5 years 3 months, was admitted into the National Hospital under Dr. Collier in February, 1907, with inability to walk and clumsiness of the upper limbs. The parents were healthy, and there was no history of family disease. There were seven children of the family, of which the patient was the fifth. Two of these had died in early infancy of blood-poisoning and of whooping-cough and convulsions respectively. The other children were healthy. The mother has had good health during the pregnancy, and birth was natural and easy. The child was breast-fed till 15 months old. From the time of birth the mother noticed that he could put his limbs into extraordinary positions, quite unlike her other children, and that his legs were very weak. He was late in attempting to stand, and never accomplished more than standing up when holding on to anything. He could never walk alone. His ability to stand when supported lasted only two months, when with increasing bodily weight he seemed to become weaker and weaker on the legs. On admission he was a pale, thin, starved-looking child of average height. His intelligence was unusually good for his age. The special senses and cranial nerves were normal. The facial musculature was well developed and symmetrical, and the facial movements were good. There was no difficulty in speaking and swallowing, and the tongue, which was protruded straight, was normal in size.

All the muscles of the upper extremity were below the normal size, but all voluntary movements could be performed with fair range and power. There was most absolute hypotonia of all the muscles, with marked relaxation of all the ligaments, so that the joints were all flail-like. The upper limbs could be folded behind the back and could be put into many extraordinary positions without causing the least pain. The muscles of the neck and of the trunk were thin and weak. He could only just raise the head from the bed when lying in the supine position, and he sat up with difficulty, the body being bunched up with a tendency to kyphosis. The respiratory muscles were unaffected. The muscles of the lower limbs were flabby, but they had a firmer feel than those of the upper limbs. There was slight contracture of the flexors of the hips and of the hamstrings, and a more decided contracture of the muscles of the feet, giving rise to a considerable degree of pes cavus. All voluntary movements were possible and were of fairly good range, except in so far as they were hindered by the contractures; and the power was fair, but the extensors were relatively weaker than the flexors. The excitability of

the muscles to faradism was much diminished, and the child showed no signs of pain when strong faradism was applied. The reaction to galvanism was normal, sensibility was normal, and there was no affection of the sphincters. The superficial reflexes were normal; the deep reflexes were entirely absent.

Under treatment this patient improved considerably and gained the power to stand and to make an attempt to walk with assistance.

Two years after his admission into the National Hospital, and when aged 7, he was attacked with pneumonia and was admitted into St. Bartholomew's Hospital, where he died after a few days' illness. The autopsy was performed by Dr. Langdon Brown in the presence of one of us.

Case 2.—H. K., a little boy, aged 3½ years, was admitted into the National Hospital under Dr. Collier in June, 1908, for inability to stand and walk, and for weakness and limpness of the limbs which had been noticed since soon after birth. He was the fifth and youngest child of healthy parents, and the other children were strong and well. There was no history of any similar disease in any relations. The birth was natural and occurred at full term. From the time of birth his mother noticed that she could put his napkins on much more easily than those of her other children, because his legs went into the right position for this operation so easily, and because he did not kick like the other children. She noticed no other peculiarity till the child was a year old, when she tried to stand him up and found that the legs doubled up anyhow under him. He was never able to stand or to walk, but when 18 months old he learnt to creep round the table by wriggling his body about. As he got older and heavier he lost this accomplishment. He could sit up, but his back bunched up in so doing, and the least touch sent him over, and when over in any direction he could not of himself regain the sitting position. He could not turn in bed or move his legs from the position in which they were placed.

On examination the child was found to be well proportioned and, with the exception of some of the limb muscles, well developed and of good weight. He was very intelligent, and was forward for his age. The special senses, optic discs, and cranial nerves were not affected. There was no affection of the muscles of the face and jaw, and swallowing was normal. There was no obvious wasting of the muscles of the neck, but these were obviously very weak, for the child never sat with his head upright, but it fell about in any direction. The muscles of the back and of the abdomen were very weak. There was a marked general kyphosis of the spinal column in the sitting position, which at once straightened out if the child were raised by the shoulders. He could not raise himself when lying down nor turn in bed. The diaphragm and intercostals acted well, as seems to be the invariable rule in this disease. In the upper extremities the muscles had a peculiar soft, homogeneous feel and could not be differentiated by touch from the overlying skin and subcutaneous tissues. They were small, but they were equally small throughout the limb, and there was no local muscular wasting, such as is always present in the true myopathies. Passive movements at all the joints were very free. Con-

siderable hyper-extension was possible at the elbow-joints, and this was very conspicuous at the wrist- and finger-joints. If the arm was held at the elbow and shaken the flail-like movements of the hand and fingers were striking. The power in the upper extremities was very poor, and he could make few useful movements with the hands. In the lower extremities the muscles were even smaller and softer than in the upper extremities, but there was no local wasting. There was apparently no volitional movement either at the hip or at the knee, but slight movements at these joints could be obtained reflexly by tickling the soles of the feet. All movements of the ankles and of the toes could be performed, but with very little power. The hypotonicity of the muscles of the thighs and of the calves was very pronounced, and the feet could easily be touched together behind the head. There was a little contracture of the calf muscles and of the hamstrings. The hyper-extensibility of the ankle (so that the dorsum of the foot is in contact with the front of the tibia in the position of rest) that has been a feature of so many of the recorded cases was not present in this case, neither were the feet conspicuously long and padlike.

The sphincters were not affected. The deep reflexes were persistently absent. The superficial reflexes were of normal type. Sensibility was unaffected. There was no lowering of sensibility to the faradic current, as has been observed in many of the cases. The child objected so strongly to the application of the faradic current that no satisfactory examination of the electrical excitability of the muscles was made, but it was obvious that the faradic excitability was much lowered in the affected muscles. The child remained in hospital for many months, and he was treated with careful feeding, massage and passive movements, in spite of which he was obviously weaker in the affected regions at the time of his discharge than he was when admitted. On the other hand, there was no extension of the muscular weakness to regions previously unaffected. With the consent of the parents a portion of the hamstring muscles was removed from the right thigh under general anæsthesia, and an account of the changes that were found in these muscles, follows in the pathological description. It must be here pointed out that no abnormality of the thyroid gland or of the thymus was clinically detectable, and that there was no œdema present at any time.

Remarks:—This was a typical case of amyotonia congenita of somewhat severe degree. The distribution of the affection followed that of the classical cases. The degree of affection of the thigh muscles, in which paralysis was practically complete for volitional movements, was extreme and unusual, and such severity of muscular affection has not been previously recorded. The pathological examination of the muscles was made when the disease had existed for rather more than three years, as compared with seven years in Case 1. This is one of the only two cases that have come under our observation in which progressive deteriora-

tion has occurred. In all our former observations there has been progressive improvement.

Pathological Examination.—The morbid changes found in the portion of muscle excised from Case 2 may be dealt with first, as in this case an earlier stage of the disease is represented. When the biceps cruralis was exposed at the operation for the removal of the muscle it appeared remarkably pale and was evidently much infiltrated by fat; in fact, very little muscular tissue could be recognized by the unaided eye. The portion excised was immediately placed in Zenker's fluid for fixation and hardening, and then, after dehydration, it was embedded in celloidin and sections 10 μ thick were easily obtained. Small pieces of the muscle were, in addition, mordanted in Müller's fluid in order that

FIG. 1.

Photomicrograph of a transverse section of the muscle. It shows (1) irregular small atrophied fibres; (2) enlarged or hypertrophied fibres which are generally circular in outline; (3) dense strands of connective tissue that run through the muscle.

the myelinated intramuscular nerves could be examined by Weigert's method. The sections of the celloidin material were stained chiefly with hæmatoxylin and Van Gieson's picro-fuchsin.

Muscle Changes.—A few bundles of normal fibres were found in the piece of muscle excised, but they occupied only a very small proportion of the cross-section. The most prominent change was an extreme smallness of the muscle fibres. In a majority of the muscle bundles not

a single fibre approaching the normal in size could be seen; indeed, their average diameter was from 6 to 12 μ, though a few of the small fibres exceeded this considerably. The contour of these small fibres in cross-section was irregular and, as a rule, oval or round; even where they were densely packed together they never presented the polygonal or facetted appearance which characterizes the normal skeletal muscle

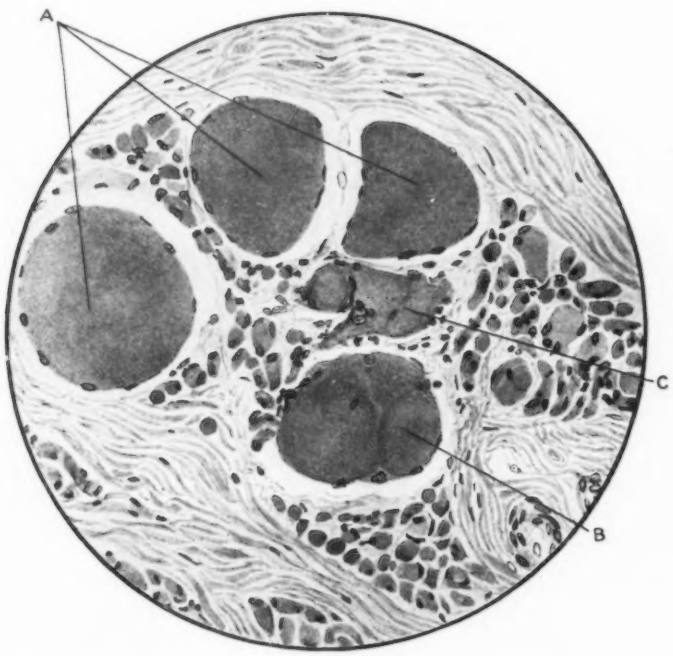

FIG. 4.

A drawing of a transverse section of the muscle: it shows the irregular size and shape of the smaller fibres, and that in many of them the sarcolemmal nuclei are proliferated. *A*, three hypertrophied fibres that are apparently normal in structure and contain only peripheral nuclei. *B*, an enlarged fibre, containing central nuclei, which is beginning to divide. *C*, an enlarged fibre that is already partly broken up.

fibre when seen in cross-section. In specimens in which these small fibres were cut longitudinally they were seen to be fairly uniform in calibre and their cross-striation was well preserved. In many of the small fibres there were scarcely more nuclei than may be found in normal adult fibres, but in some there was a marked proliferation of

the sarcolemmal nuclei, and in places this was so great as to conceal the substance of the fibre. No degenerative or regressive changes could be made out in these small or atrophic fibres.

A still more striking feature of the appearance of cross-sections of the muscle was the presence of numerous relatively enormous fibres which were generally of circular outline in cross-section, and which measured from 100 to 150 μ in diameter. These greatly enlarged fibres generally lay isolated in or among the bundles of small fibres; they were only rarely found forming bundles of themselves. Apart from their size and their unnaturally cylindrical shape, the greater number of these giant fibres appeared to have a normal structure and contained

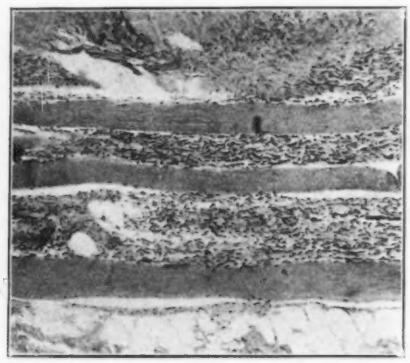

FIG. 2.

Photograph of a longitudinal section containing three hypertrophied fibres, separated by small or atrophied fibres in which there is a considerable increase of nuclei.

nuclei only immediately under the sarcolemmal sheath. Their cross-striation was distinct, but in many of them the longitudinal striation was unduly prominent. In a certain proportion, however, of these giant fibres unmistakable regressive changes were present; some of them contained central nuclei either embedded in normal myoplasm or surrounded by a zone of undifferentiated sarcoplasm. Occasionally the muscle tissue immediately surrounding the central nuclei had a remarkable tendency to take a deep but diffuse stain with hæmatoxylin. In other fibres the regressive process had gone still farther and lead to central vacuolation and splitting up of the fibre, while in some the myoplasm was more or less disintegrated and invaded by the

sarcoplasm and sarcoplastic nuclei. In longitudinal sections portions of these fibres could be seen transformed into protoplasmic masses pervaded by nuclei, the sarcolemmal sheath generally remaining intact. The central vacuolization resulted, in many fibres at least, from the fusion of a series of small discrete vacuoles in the walls of which nuclei were frequently present. In longitudinal sections it could be seen that a few of the enlarged fibres were splitting up longitudinally into apparently well-formed fibres of small calibre, provided with a normal sarcolemmal sheath and nuclei (fig. 5).

The muscle was also characterized by the great increase of connective tissue which was arranged both in massive bundles running

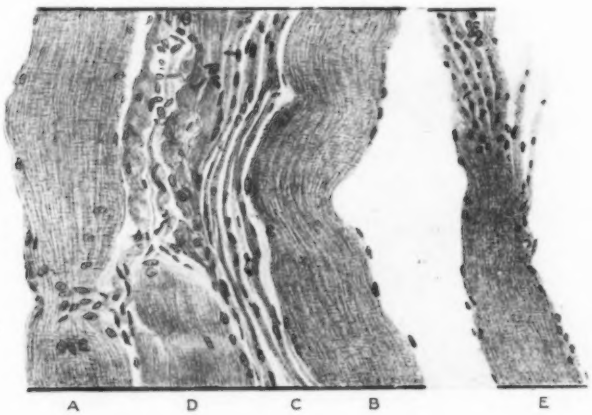

FIG. 5.

Drawing of a longitudinal section. *A* and *B*, hypertrophied fibres which are normal in structure; *D*, one that contains central nuclei and is breaking up by longitudinal fission. *C*, slender atrophied fibres. *E*, an hypertrophied fibre that is splitting longitudinally.

between and surrounding the muscle bundles, and in very delicate strands of connective tissue which in places even penetrated between the individual muscle fibres. There was also a notable determination of loose fatty tissue between the muscle bundles, and to this the remarkably pale naked-eye appearance of the affected muscle was due. The muscle spindles were on the whole normal, but in places their sheaths appeared slightly thickened.

Considerable thickening of the walls of many of the blood-vessels was a noticeable feature of many of the sections. This was the result chiefly

of a periarteritis, but there was also some proliferation of the intimal cells. A few foci of small round-celled infiltration were found, which generally lay in immediate relation to a vessel, but these were only rarely met with in a large number of sections examined.

In the sections of muscle stained by Weigert's method there seemed to be remarkably few myelinated nerves, and the myelin sheaths of those that were present seemed poorly developed.

In Case 1 death occurred from pneumonia, and a complete autopsy was made. There was no abnormality of the thyroid, thymus,

FIG. 3.

Photograph under a low magnification to show the excess of fat and connective tissue the muscle contains, as well as the small size of its fibres; one hypertrophied cylindrical fibre lies in the centre of the figure.

or spleen found, and, with the exception of the lungs, the internal organs appeared natural; the muscles of the affected regions were small and very pale, and contrasted very sharply with the muscle of the diaphragm, which was not affected. The muscles were fixed in Zenker's fluid, the peripheral nerves in Müller's fluid, and the central nervous organs as well as the other organs were placed in a 10 per cent. solution of formalin in normal saline solution.

Muscle Changes.—The changes in the muscles were very similar to those found in the preceding case. The most striking difference was

a greater proliferation of the sarcolemma nuclei in the small fibres, many of which were almost concealed by continuous columns of nuclei arranged along them. Further, in many places sarcoplastic nuclei could be seen lying apparently free in the connective tissue. The large hypertrophied fibres so conspicuous in the other case were much less numerous and less prominent in this case. There was also a greater amount of connective tissue in the more severely affected portions of the muscles, and it was more densely sclerosed. In places, too, there was a remarkable deposition of fat, so that portions of the muscle seemed to be completely replaced by fatty tissue.

The pathological changes, however, varied considerably from muscle to muscle, and even in different portions of the same muscle: the diaphragm, for instance, was unaffected, and the biceps brachialis was much less severely affected than were the pectoralis major and the semitendinosus. This indicates a definite parallel between the degree of the clinical symptoms and that of the pathological changes in the muscles.

Peripheral Nerves.—The external popliteal and the median nerves were preserved for microscopical examination. In sections stained by Weigert's method the nerve fibres in cross-section seemed rather far apart, and the myelin sheaths of a small proportion of the fibres were poorly developed. On macroscopical examination it was obvious that the ventral spinal roots throughout, but more especially those of the lumbo-sacral region, were remarkably slender in relation to the size of the dorsal roots, and this appearance was confirmed by their examination in Weigert preparations; for under the microscope their fibres appeared not only much reduced in number, but individually slender and poorly myelinated.

Spinal Cord.—The white matter of the spinal cord showed no abnormalities and the fibres were well myelinated. On the other hand, Nissl preparations revealed unmistakable pathological changes in the ventral horns at all levels of the spinal cord. The large cells of the motor type were much reduced in number, in places there appeared to be scarcely one-third of the normal number of these cells present, and those that were present were individually smaller and more angular and irregular in shape than are normal cells. These changes were found in all regions of the spinal cord, but they were most conspicuous in the lumbar and sacral segments and in the lower segments of the cervical enlargement. In the cervical enlargement it was the lateral and the postero-lateral groups of cells that were the most severely affected. The cells of the dorsal horns and those of Clarke's column were normal.

It is now necessary to compare these pathological changes with those that have been already discovered in similar cases. But till now only Bing, Spiller, and Baudouin have had the opportunity of recording such observations. These have been already abstracted and analysed by one of us with Dr. S. A. K. Wilson [4].

Bing's [3] examination is the least important, as he had only a very small piece of muscle removed during life, and in its fibres he found only an increase of nuclei.

Spiller [6], who made a *post-mortem* examination on a case that died at the age of 22 months, found the muscles pale and infiltrated by fat, the muscle fibres small, and a considerable increase of the nuclei of the connective tissue. The peripheral nerves, the dorsal and ventral spinal roots, and the central nervous system were normal. The report, especially of the muscle changes, is not as complete as could be wished.

Baudouin's report [2] is much fuller. In a child that died at the age of 4 months the muscle was largely replaced by fat and contained a considerable excess of connective tissue; the majority of the fibres were atrophied and contained a large number of nuclei, but others were enormously hypertrophied, measuring up to 100 μ in diameter, and were often penetrated by sarcoplastic nuclei. Some of these hypertrophied fibres were found splitting longitudinally. There was also a considerable diminution in the size, and perhaps in the number too, of the ventral horn cells, and the ventral roots of the spinal cord were less than half the normal size and were poorly myelinated.

From these short abstracts it is evident that the pathological changes in the muscles in Baudouin's case were practically identical with those present in the two cases we have been able to examine, and there was an equally striking similarity between the alterations in the peripheral nerves and the ventral horns of Baudouin's case and in our case that came to *post-mortem* examination. The changes Spiller found in the muscles do not differ essentially from those we found, though he does not refer to the presence of hypertrophied fibres. In the nervous system, on the other hand, he found no pathological changes. These discrepancies may be perhaps explained by a difference in the intensity or the stage of the disease.

There is not much difficulty in interpretating these muscle changes. The most common, constant, and characteristic change was the smallness of the majority of the muscle fibres. This smallness may be, on the one hand, attributed to a non-development of these fibres, or on the other to regressive or atrophic processes affecting them. The latter seems the

more likely explanation, as the extraordinary irregularity in the size and shape of the fibres could be hardly expected if the smallness was merely due to an arrest of development; and the considerable increase in their nuclei and the presence of apparently free nuclei in the connective tissue are much more in favour of the view that they arise by the regression of normal fibres. Further, it must be remembered that in places we found small fibres arising by the longitudinal fission of large fibres. Finally, the appearance is not that of undeveloped fibres; it is only towards the end of the sixth month of intra-uterine life that the central portions of the skeletal muscle fibres become differentiated and that the nuclei move to the periphery of the fibre, and they receive their sarcolemmal sheaths only at the time of, or shortly before, birth. But in all the muscles we have examined the central portions of all the small fibres were fully differentiated, and they possessed well-developed sarcolemmal sheaths.

The significance of the large hypertrophied fibres is more difficult of interpretation; it has been much discussed in relation to the myopathies, in which there are found similar large fibres certainly identical with those we describe here. Erb regarded the increase in size as a true hyperplasia preceding atrophy, while Dejerine has attributed it to a vicarious functional hypertrophy. Whatever may be their nature, the active regressive changes we have already described in them must be regarded as unequivocal evidence of a progressive pathological process.

The clinical features of the disease are easily correlated with the pathological changes we have found. The great atrophy and the decrease in number of the muscle fibres sufficiently explain the palsy, while the infiltration of the muscles by fat and the increase of connective tissues in them concealed in part the general atrophy. The atony may be attributed to the same cause, while the contractures that occasionally develop are evidently due to sclerosis of the fibrous tissue that is laid down in the muscles.

The fact that some cases improve has been regarded as one of the features of the disease. From the pathological point of view, however, improvement appears unlikely; we detected no evidence of regenerative or reparatory changes in the muscles, but the possibility that the atrophic fibres may regain their normal size and function must be admitted. But for the muscle to regain its proper function it appears necessary that the excess of fat and the fibrous tissue that is found, both in thick bundles and in fine strands, between the affected fibres should be absorbed or removed. This certainly does not appear likely.

In this connection we must again refer to the active regressive changes that were present in a considerable proportion of the enlarged fibres.

Finally, there remains to be considered the relation of the morbid anatomy of these cases to that of the myopathies. On comparing the muscle changes found in these two conditions, we must admit that there is no essential difference, though in our younger case there was, perhaps, not so great an increase of nuclei in the atrophied fibres as is generally present in the myopathies. Myopathic muscles are characterized by the presence of atrophied and hypertrophied fibres, with a proliferation of their sarcoplastic nuclei and various regressive changes in them, an increase of connective tissue and a deposition of fat; and it is exactly the same changes we record above. Further, we observed a thickening of the vessel walls which is almost constant in myopathic muscles, and the collections of small round cells which have been referred to are similar to those that may be seen in myopathic muscles.

Baudouin came to the same conclusion, for he wrote of the muscular alterations in his case as "les lésions de la regression musculaire telles qu'on peut les voir dans les myopathies."

It must be pointed out that the spinal changes observed by Baudouin and in one of our cases do not constitute an essential difference from the pathology of the primary myopathies, for one of us [5] has recorded a case of the juvenile form of muscular dystrophy in which practically identical spinal changes were present, and in that paper there are collected together a considerable number of similar cases that had been previously reported. Ballet and Laignel-Lavastine [1] have more recently published a similar observation.

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(A complete bibliography of the subject will be found under Reference No. 4.)

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AN EPIDEMIC OF ACUTE POLIOMYELITIS.[1]

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EPIDEMICS of acute poliomyelitis have seldom been recorded in England; in fact, of thirty-two epidemics described in medical literature, two only occurred in this country. The records of Swedish epidemics show that poliomyelitis must be far commoner in some other countries than it is in England. But, apart from a greater frequency of the disease, the segregation of the population of this country in large towns makes it more difficult to define the epidemic nature of the disease. Thus, although a few years ago it was well recognized that a large epidemic was occurring in London, the great difficulty in collecting the different cases rendered abortive all attempts to trace the epidemic. Although it would be impossible to add to the wonderfully painstaking descriptions of the Swedish scientists, yet we believe that an account of even a small epidemic in England is worthy of notice, in that it brings the disease in England into line with the disease as it occurs in other countries, and affords the opportunity of comparing its similarities and differences.

Thirty-two epidemics of poliomyelitis have been recorded, the first (an epidemic of eighteen cases) by Bergenholf, in November, 1881 [11]. The first large epidemic was reported by Caverly in 1894 [4]. It consisted of 136 cases, and occurred in an area of 15 miles in Rutland. It occurred during a very hot summer and was associated with cases of paralysis among cattle and fowls. Eighteen patients died, and in six cases there were constitutional symptoms without any paralysis. Unfortunately no autopsies were performed, and it was considered by some authorities to be epidemic cerebrospinal fever. There was, however, no purpuric eruption, and it seems (judging by later epidemics) to have been undoubtedly acute poliomyelitis.

[1] My best thanks are due to Dr. Dunlop, of Upminster, under whose care were most of these patients, for the kind way in which he aided me in tracing this epidemic.

Of the two epidemics recorded in England, one, recorded by Buzzard [3], consists of four cases. Two sisters living in the same house were attacked within six days of one another, and also two other children (who were not examined) living in the same street.

The other epidemic was recorded by Pasteur [12], and is of the greatest interest. In July, 1896, the whole of a family of seven children were attacked with fever within ten days; in three cases the fever was followed by paralysis, and by other nervous symptoms in the other four cases. The eldest child, Herbert George, aged 11, five days after the onset of the fever was paralysed in the left arm, and had a transient paralysis of the right side of his face and palate. The second child, Samuel James, aged 9, after seven days of fever was found to be suffering from rigid hemiplegia on the right side. The two next children, George, aged 8, and Edith, aged 6, had fever resembling that of the others, but did not develop any nervous symptoms. Alice, aged 5, after five days of fever was paralysed in the left leg, which was at first rigid below the knee. Philip, aged 4, and Eva Mary, aged 18 months, after a few days of fever were seized with tremors which lasted some days; the youngest child also had strabismus of short duration. The illness with which they were all affected was characterized by pyrexia and headache; there was no rash, nor any sensory changes. There were no epidemics in the village at that time.

Of other epidemics, those recorded from Norway and Sweden are of the greatest importance owing to the pains taken by Wickman and his colleagues to investigate the disease thoroughly from all aspects. In those countries thirteen epidemics in all have been reported, but by far the largest are those investigated by Wickman [15]. He had carefully worked out the details of four epidemics, one of them consisting of over 1,000 cases.

The first occurred in the summer of 1899, and consisted of fifty-four cases; the second of twenty cases in 1903; the third in 1905, numbered 1,031 cases; and in 1906 there was an epidemic of fifty cases. These epidemics all occurred in hot, dry summers, and the number of affected persons reached its maximum in August. The patients were mostly children, but the maximum age-incidence was not so low as in some of the other epidemics; the greatest number were between 3 and 5 years of age, but the disease attacked large numbers of children up to the age of 8. Many adults were, however, attacked, the oldest patient being aged 65, and the mortality was far higher among the elder children and adults than among the younger children. In the large epidemic of 1,031

cases there were 135 deaths, the average mortality of children under 10 years being about 11 per cent., and of the older patients about 26 per cent. Many patients exhibited symptoms of acute polio-encephalitis, either apart from or in association with the ordinary spinal symptoms, and many patients had the constitutional symptoms without subsequent paralysis. To see what light is thrown upon the subject by Wickman's investigations it will be best to consider them under three headings—pathological, etiological, and clinical.

Autopsies were made imperative upon all patients dying during the epidemics, and in this way much valuable material was obtained. All the fatal cases were carefully examined by Harbitz and Scheel [8]. They found that there was a patchy lepto-meningitis more evident on the anterior aspect of the cord, and most severe near areas where the deeper nerve-structures were involved, and that there was great engorgement of the pia in affected areas. The changes in the anterior cornua of affected areas were found to be the same as described by other writers. Harbitz and Scheel, however, regard the lepto-meningitis as the primary lesion, and believe that the inflammatory condition passes in along the vessels, affecting the interstitial tissue and then the large ganglion-cells which derive their nutriment from these vessels. The fact that the inflammation is hæmorrhagic is probably due to the softness of the cord rather than to the severity of the inflammation, as inflammatory changes in any soft organ—as, for instance, the pancreas—tend to be accompanied by hæmorrhage.

As regards the etiology, Wickman proved conclusively that it must be bacterial. He traced several cases where a healthy individual, after visiting an affected centre, returned home, and, having developed the disease himself, infected other people in the previously immune locality. Cases like the above, and also the fact that during the epidemics many patients were affected with paralysis without any febrile symptoms, leave no doubt that acute poliomyelitis (whether developing with febrile onset or coming on without any warning) as a clinical entity is due to some bacterial action. Many different micro-organisms have been separated at different times. Geirswold [5], who investigated the epidemics from the bacteriological point of view, found a poorly staining diplococcus. He could not prove this organism to be the specific organism of the disease, as it was never found alive but undergoing bacteriolysis, and he thought that though a similar organism has not been discovered in any other disease, yet it might be only a coincidence and not the specific organism.

To the clinical knowledge of the disease epidemiology has added much. The first fact of interest is, of course, that it does occur in epidemics, and that these epidemics always occur during the hot summer months. Secondly, that the disease is spread by human beings. The time of year at which all the epidemics have occurred would suggest an analogy with epidemic summer diarrhœa and vomiting, but the way in which Wickman was able to trace the spread from village to village shows that the infection must be born by human beings and is not due to bacterial infection of food.

A third point emphasized in the epidemics was the almost universal febrile constitutional symptoms. In many cases paralysis did occur without any constitutional symptoms, but so well recognized were the premonitory symptoms that doctors were able to predict the likelihood of paralysis in a child who only showed symptoms of general malaise.

But perhaps clinically the most interesting feature was the occurrence of many cases which, though not typical poliomyelitis, were obviously other manifestations of the disease which usually attacked the anterior cornua.

Wickman divided the cases into the following clinical types :—

(1) *Spinal poliomyelitis.*—Cases resembling the acute anterior poliomyelitis of text-books. This class was far the largest.

(2) *Ascending myelitis.*—The inflammation rapidly ascending until it affected the basal nuclei; these cases clinically resembled Landry's paralysis.

(3) *Bulbar or pontine cases,* involving the basal nuclei, were generally soon fatal.

(4) *Encephalitis.*—The cerebral cortex was attacked; these cases were identical with superior polio-encephalitis.

(5) *Ataxia.*—A few cases with ataxia resembling Friedreich's ataxia.

(6) *Polyneuritis.*—Many cases, as observed by Gowers [7] and many others, of acute poliomyelitis have symptoms of polyneuritis. This peripheral neuritis causes great local tenderness and appears to be severest in the middle of the course of the nerve.

(7) *Meningitis.*—Many cases of acute poliomyelitis exhibit symptoms of meningeal inflammation. They develop usually before the paralysis and pass off fairly soon. In some cases, however, the symptoms of meningeal irritation were the only symptoms pointing to any spinal lesion.

(8) *The abortive form,* where no paralysis developed, although con-

stitutional symptoms were present exactly resembling those of other patients who were subsequently paralysed. Wickman divides these into three types: (1) General malaise; (2) meningeal irritation; (3) resembling the gastro-intestinal type of influenza.

The occurrence of so many different forms show that though the bacterium or its toxin has a predilection for the anterior cornua, yet it can attack the central and peripheral nervous system at almost any point.

There have been three other large epidemics of late years: one in Queensland in 1903 [10], one in New York in 1907, and one in Melbourne in 1908.

The epidemic in New York [1] [6] [14] was probably the largest that has ever occurred. It was estimated to number several thousands, but unfortunately no careful records were kept. It occurred at the end of a hot, dry summer, and seems in the main to have shown the characteristics of the other large epidemics.

The epidemic in Melbourne was carefully investigated by Douglas Stephens [13]. There were 137 cases and 6 deaths. The summer had been hot and dry, and the largest number of cases occurred towards the end of August. Stephens carried out his investigations as far as he could on the same lines as Wickman.

He considered the disease to be mildly contagious, and suggested that the prominence of gastric or respiratory symptoms might point to different sites of infection. He was, however, unable to prove that point.

In the Melbourne epidemic the cases seem to have assumed the same clinical forms as those described by Wickman. On bacteriological examination a poorly staining diplococcus resembling that described by Geirswold was found. In addition, an organism was isolated resembling the *Staphylococcus pyogenes aureus;* it was not pyogenic, and produced no symptoms on inoculation into the spinal cord of a guinea-pig.

More recently experiments have been carried out by Landsteiner and Popper [9] with material from a case in Vienna. A boy, aged 6, died of acute poliomyelitis within twenty-four hours of its onset. His cord showed the typical histological changes (described by Harbitz and Scheel), but, on staining, no micro-organisms were seen. Cultures taken on agar, serum-agar, and blood-agar were negative. The substance of the cord was inoculated into two rabbits, two guinea-pigs, two mice, and two apes. With the exception of the apes, none developed any symptoms or showed any *post-mortem* lesions. One ape developed typical paralysis after seventeen days and died two days later. With the cord of this animal two other apes were inoculated,

but without any result. The other monkey was taken very ill six days after inoculation, and died two days later; but, although the cord was much inflamed, there was no typical paralysis.

From these experiments they suggest that the organism is probably too small to be seen.

An epidemic of acute anterior poliomyelitis occurred in the village of Upminster in the summer of 1908. It consisted of eight cases, and lasted from July to September.

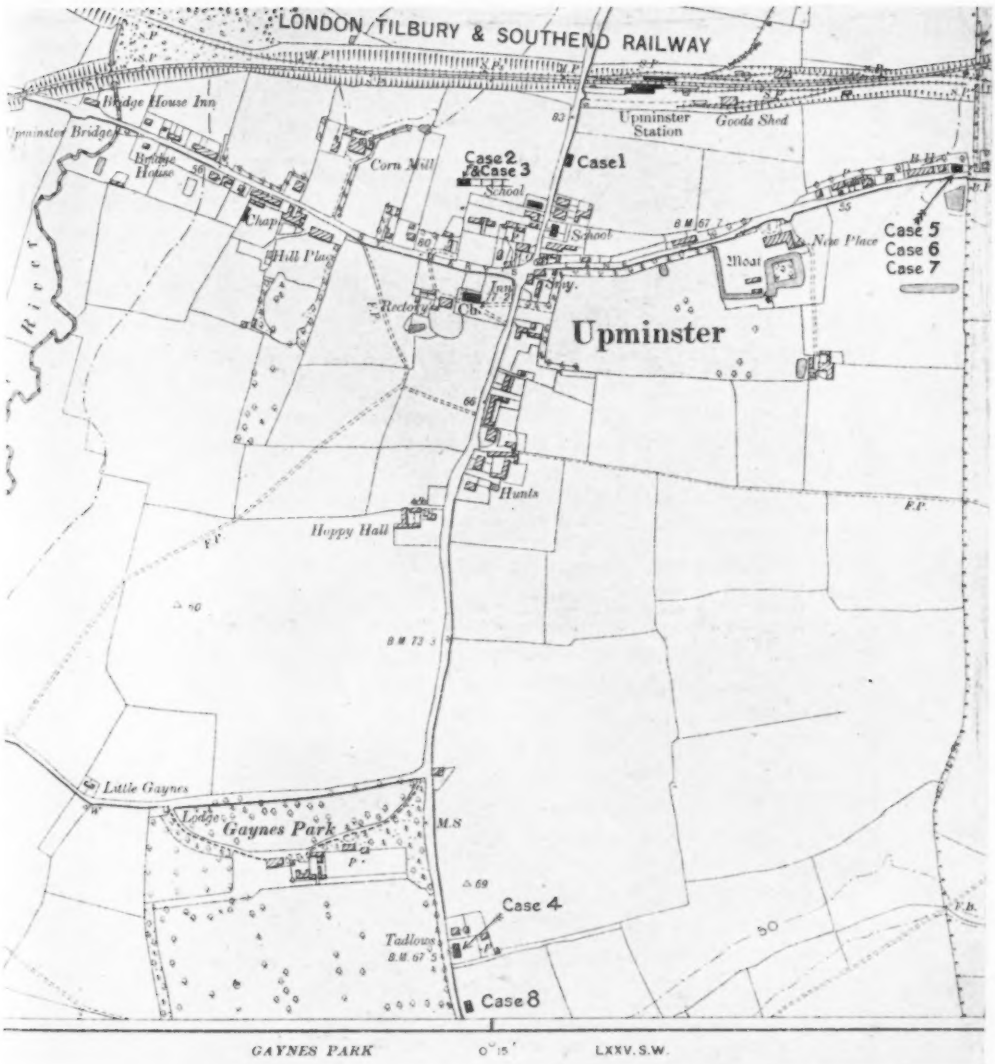
Upminster is a small, straggling village in Essex on a clay soil, with a population of 1,477. It is an agricultural district, and is in no way brought into contact with any country, such as Norway or Sweden, from which infection might have been conveyed. There has never been any similar epidemic in the village, and no case of infantile paralysis has occurred there for several years. The locality has always been considered healthy, and there was no epidemic of any other disease during the year 1908. The months during which the outbreak occurred were hot and dry, but the heat was not excessive.

The first child to be attacked was Gertrude H. (Case I.), aged $3\frac{1}{2}$. She was taken ill on July 27; she was sick, had pains all over her body and a bad headache, and a temperature of 101° F. [38·5° C.]. On August 3 she was found to be paralysed. When examined in February, 1909, she had an almost complete flaccid paralysis of both lower limbs, and was quite unable to stand.

On August 24 three more children were affected: two sisters, Enid (Case III.) and Maud H. (Case IV.)—who, although they bear the same surname as the first patient, Gertrude H., are in no way related to her, and a boy, John C. (Case II.).

John C. (Case II.), aged 13, was taken ill on August 24. He was feverish, his eyes were "glazed," he vomited, and had pain in his lumbar region when moved. He stayed in bed three days, and on August 27, when he got up, fell owing to the weakness of his right leg. The muscles rapidly wasted, and in February, 1909, there was a flaccid paralysis of most muscles of the right thigh and leg.

Enid H. (Case III.), aged 11, and Maud H. (Case IV.), aged 12, had returned to Upminster from Westgate on August 18. On the afternoon of August 24 both sisters were feverish and had pains in the head and stomach. They did not go to bed. The next day they were seen by Dr. Dunlop, and had sore throats and a



Map of the district in which the epidemic occurred. Taken from the Ordnance Survey [6 inches to one mile, or about 1 cm. to 105 metres].

temperature of 101° F. [38·5° C.]. They were sent to bed. Maud got quite well in three days and never developed any paralysis. Enid, between August 28 and 30, had three attacks like severe cramp in the left leg, and on August 30, when she tried to get up, fell, as both legs were weak. When seen in February, 1909, the right leg appeared normal, but the left leg was much wasted and many of the muscles were still paralysed.

The next children to be attacked were three of the M. family. The whole family had been away to Gatestown and returned to Upminster on September 3. The three affected were the middle members of the family, the eldest and youngest remaining well.

The first to fall ill was Stanley (Case V.), aged 8. On September 9 he had a cough, bad headache, was feverish, and had staring eyes. On September 11 it was noticed that he was completely paralysed in his left arm. He rapidly made a partial recovery, but in February, 1909, there was still a flaccid paralysis of many muscles of the left arm. His sister, Eva Rose M. (Case VI.), aged 10, was taken ill September 11, the day after her brother, with similar symptoms. On September 13 she had lost all power in her neck. Within three weeks she had almost entirely recovered, and in February, 1909, no paralysis was detected.

On September 12 Gladys M. (Case VII.) had a bad headache, vomiting, feverishness, and general malaise. On September 14 she had completely lost the use of both lower extremities. She partially recovered the use of her left leg, and in February, 1909, it appeared quite normal, but there was a flaccid paralysis of most muscles of the right thigh.

The last case was a boy, Basil J., aged 13 (Case VIII.). On September 16 he suddenly became paralysed in his right leg. There was a history of a knock several days previously, but he had been quite well since and the blow was not a severe one, and it seemed justifiable to disregard it. The paralysis came on without any constitutional symptoms. In eight days the leg was quite recovered, and in February, 1909, there was no sign of any paralysis.

Fortunately, though only a small epidemic, it includes all the three clinical types of the large epidemics. Six of the children had constitutional symptoms and then a few days afterwards became paralyzed; one child (Maud H.) had the fever, but developed no paralysis; while Basil J. was paralysed without any constitutional disturbance.

The distribution of the paralysis agrees with the general descriptions, the legs being most commonly affected. In some of the children the eyes seem to have attracted the parents' attention by their peculiar

look, but in no case was any definite evidence of polio-encephalitis obtained.

The age of the patients is of interest. All were over 6 years of age, except Gertrude H., who was 3½ years old. About 60 per cent. of all cases of acute anterior poliomyelitis occur in the first three years of life, and, with the exception of Gertrude H., in each family there were younger children who escaped the disease.

As regards the incubation of the disease, the periods of which any information could be gained agree with the figures of Wickman. The child in whom the disease first started had not been out of Upminster, and so the disease must have originated in that village. Enid and Maud H. returned on August 18 and were attacked on August 24; the M. family returned on September 3, and the first was taken ill on September 9: so that in these cases the incubation could not have exceeded six days.

In other epidemics it has not been common for more than one member of a family to be affected, but in this case there were three in one family and two in another. All attempts to trace the means by which the disease spread failed.

Case I.—Aged 3½. *Taken ill with pains in the head and vomiting on July* 27, 1908. *Paralysis discovered on August* 3. *Examined February*, 1909; *then had flaccid paralysis of both lower extremities and lower part of spine.*

Gertrude J. H. on July 27 fell asleep while out of doors in the evening. She was brought home at 7 o'clock and vomited when she woke up. She was put to bed, but got up next morning. She had severe pains in the head and had to be carried downstairs. On that day she vomited again. The following day, July 29, Dr. Dunlop was called to see her. She had pains in her head and pains all over when she moved. At that time there was no paralysis. On August 3 it was discovered that she was paralysed in both her lower extremities. The paralysis had never been more extensive than it was when she was examined in February, 1909.

She is the youngest of a family of six children. The other children were all at home at the time of her illness, and she was nursed by her two eldest sisters. None of them had any illness at that time. She had not been away from Upminster at any time shortly before her illness.

Condition in February, 1909.—She was a largely-built child, looking about her age. She had always been healthy, and there were no abnormal signs in the heart, lungs, or abdomen. There was obvious wasting of both lower extremities. There was a definite curve in the lumbo-sacral region and wasting of the lower part of the erector spinæ. There were no cutaneous nor vasomotor changes. She could sit up by herself, but was

unable to stand. She could extend and flex the toes of her left foot, and could adduct but not abduct the left foot. With the exception of these movements there was complete flaccid paralysis of both lower limbs. The tibialis anticus, the peroneus longus, and the peroneus brevis of the left foot appeared to be unaffected. The extensors and flexors of the toes and foot on that side were working, but appeared to be weak. With the exception of these muscles there were great wasting and loss of tone of all the muscles of both lower extremities. The glutei on both sides were affected, and also the lower part of the erector spinæ. As the child was frightened the electrical reactions could not be tested. She was having electrical treatment, however, and the operator stated that the muscles did not react to faradism, but gave a slow contraction when stimulated by the galvanic current. The knee-jerks on both sides were absent. The plantar reflex on the left side was flexor; on the right side it was absent. Sensation appeared to be unaffected. The sphincters were unaffected.

Case II.—Aged 13. *Taken ill August* 24, 1908, *with headache and vomiting. Stayed in bed for three days. August* 27, *when he got up, his right leg was weak. Examined February*, 1909: *flaccid paralysis of right leg and thigh.*

John C. was taken ill on August 24, 1908. His head ached and he had pain in the lumbar region when he moved. He was feverish, and he vomited several times. His parents say that his eyes were "glazed." He stayed in bed for three days, and at the end of that time he felt quite well. On August 27, when he got out of bed, his right leg was weak, so that, although he could walk without assistance, he was liable to fall down. He had no pain in his leg and there was nothing peculiar to be seen. The muscles rapidly wasted both above and below the knee. He attended the London Hospital until September 26, and was treated with electricity and massage. After that date the treatment was continued at home.

He is considered the healthiest of a family of nine children, five of whom are older and three younger. The rest of the family were at home, but none of them were attacked by any illness.

Condition in February, 1909.—He was a well-grown, strong, healthy-looking boy, who had never had any serious illness before. Three years ago he was hit on the vault of his cranium by a piece of lead piping: the bone was not affected, but the scar remains, and he has occasional headaches since, but no other trouble. There were no abnormal signs in any of the abdominal or thoracic viscera. There was obvious wasting of the whole of the right thigh and leg, especially in the region of the quadriceps and psoas. The foot was in a position of slight equinus, with hyper-extension of the big toe. There were no cutaneous nor vasomotor changes. On measurement, the right leg was found to be considerably smaller than the left, both above and below the knee.

Below patella	*Right*	*Left*
10 cm.	25·7 cm.	26·4 cm.
15 „	28·3 „	29·6 „

Above patella	*Right*	*Left*
8 cm.	28·5 cm.	31·5 cm.
12 „	31·3 „	35·6 „
16 „	33·2 „	37·4 „
24 „	34·5 „	39·4 „

He could walk quite well without assistance. There was slight dropping of the right foot and updrawing of the big toe. In the right leg all the muscles except the tibialis anticus were working, but they were not so strong as in the left leg, and the extensors were more affected than the flexors.

In the thigh he could not fully flex the thigh on the abdomen, nor could he fully extend the leg. Flexion, external rotation, and abduction were good; adduction and internal rotation were weak. The psoas and quadriceps in the right thigh and the tibialis anticus in the right leg were the only muscles in which there was no action. All the muscles of the thigh, except the quadriceps and psoas, reacted well to the faradic current. The sartorius and glutei reacted well.

In the leg all muscles but the tibialis anticus reacted well to the faradic current. The tibialis anticus gave a slow action to 4 ma. of galvanic current, the contraction being greater on closure of the current when stimulated by the anode than by the kathode. No reaction was obtained to the constant current in the quadriceps or psoas with 4 ma. The knee-jerk was not obtained in the right leg; the plantar reflex was flexor. There were no sensory changes.

Case III.—Aged 11. *Illness began August* 24, 1908, *with headache and feverishness. August* 25: *went to bed, and during next five days had attacks resembling cramp in her left leg. On August* 30 *it was discovered that she was paralysed in both her legs. Examined February*, 1909: *flaccid paralysis of some muscles of left leg, but no muscle of right thigh or leg obviously affected. Sister of Case IV, but no relation to Case I.*

Enid H. had been staying at Westgate and returned to Upminster on August 18. On August 24, in the afternoon, she had a bad headache and was feverish, but did not go to bed. On the evening of the next day she went to see Dr. Dunlop. She then had a headache, slight sore throat, and a temperature of 101° F. [38·5° C.], but no paralysis. She was sent to bed. Between that time (August 25) and August 30 she had three attacks like bad cramp in the left leg. These attacks lasted about one minute, and were so severe that they made the patient scream. On August 30 she felt quite well and tried to get up, but fell. She was again examined by Dr. Dunlop. The sore throat had recovered and the constitutional symptoms had subsided. The right leg was weak, but the knee-jerk was present. The left leg was paralysed, and the knee-jerk was absent.

The right leg gradually got better. The muscles of the left leg wasted rapidly, but after a few weeks she began to regain power and could walk about.

She is the second child of a family of four children. All the children had been away together at Westgate and they all returned to Upminster on August 18. Her elder sister (Case IV.) was taken ill on the same afternoon with pains in the head and stomach, but she did not develop any paralysis. A younger sister, aged 5, and a brother, aged 18 months, were not affected.

Condition in February, 1909.—A good-looking girl, looking more than her age. She has always been healthy and has had no serious illness. There were no abnormal signs in the heart, lungs, or abdomen. The right leg was well developed and was not affected in any way. In the left leg there was obvious wasting both above and below the knee, the wasting being greatest in the front of the thigh. There were no cutaneous nor vasomotor changes. The circumference of the left leg at various levels was considerably less than that of the right leg.

	Left	*Right*
Below patella		
10 cm.	24·0 cm.	26·25 cm.
15 „	20·5 „	23·5 „
Above patella		
8 cm.	26·0 „	30·0 „
16 „	28·25 „	35·5 „
24 „	30·0 „	38·25 „

She could walk well, though she dragged the left leg slightly. The movements of the right leg and thigh were perfect. She could not extend the left knee to any material degree, and all other movements were weak. In the left thigh the quadriceps (including both vasti) were not working; the hamstrings, the abductors, and adductors were working but were weak. The glutei on both sides were perfect. The muscles below the knee on the left side were working, but were weak compared with the right side. All the muscles of both extremities reacted well to the faradic current, except the left quadriceps. The left quadriceps did not react to a galvanic current of 4 ma.

The knee-jerk was present on the right side, and absent on the left. The plantar reflex was flexor on both sides.

There were no sensory changes.

Case IV.—Aged 12, *sister of Case III., no relation to Case I. Taken ill on August* 24 *with pains in stomach and head. In bed three days. Never any nervous symptoms.*

Maud H. returned from Westgate on August 18 with her sister Enid (Case III.) and the rest of the family. On August 24 she was taken ill with headache and pains in the stomach. Her illness started rather later in the day than her sister's, and it was not so severe. She had no sore throat and no pains in her limbs. On August 25 she went to bed, as her sister had been ordered to do so. She stayed in bed for three days, and at the end of that time she felt quite well and was allowed to get up. She had no paralysis or muscular weakness.

Condition in February, 1909.—Not so strong or well-developed a girl as her sister Enid (Case III.), but quite healthy. There were no abnormal signs nor weakness in any organ or in any limbs.

Case V.—Aged 8. *September* 9 *had a cough, a bad headache, and was feverish. September* 11 : *was found to be entirely paralysed in his left arm. Improved greatly but not completely. When examined in February*, 1909, *had wasting and paralysis of many muscles of his left arm. He is the brother of Cases VI. and VII.*

Stanley M. had been away with the rest of the family to Gatestown, in Essex, and had returned to Upminster on September 3. On September 9 he had a cough, a bad headache, and "glaring" eyes. He was feverish and had lost his appetite. He was put to bed. On September 11 he did not use his left hand to feed himself, and it was found that he had lost all power in his left arm. In a few days he could lift his left arm almost to a right angle, but could not bend it nor grasp anything in his left hand. The muscles rapidly wasted. There was no rash nor vomiting, no pain, and no loss of power elsewhere. He attended the London Hospital for electrical treatment, and his condition much improved.

Stanley M. is the third child of a family of five. The whole family had been away together and returned on the same day. The eldest child, aged 14, and the youngest, aged 12 months, remained quite well. The other two, Eva Rose (Case VI.), aged 11, and Gladys (Case VII.), aged 6, were affected with constitutional symptoms, like those of Stanley, two and three days later respectively, and each subsequently developed a flaccid paralysis, but in different parts of the body.

Condition in February, 1909.—He was a healthy-looking boy, but not largely built. He had diphtheria in 1907, but has always been bright and healthy. The left hand could be held in any position, but was usually held fully pronated, the wrist dropped and the proximal phalanges hyper-extended. The first phalanges of the ring and little fingers were extended; the second and third were slightly flexed. The thumb was held extended and abducted. The muscles of the whole limb were wasted and had lost their tone, those of the hand being most affected, and those around the scapular least. There were no cutaneous or vasomotor changes.

On measurement the left arm and forearm proved to be definitely smaller than the right.

From the tubercle of the acromion	*Right*	*Left*
5·0 cm.	19·0 cm.	16·5 cm.
10·0 „	17·8 „	15·6 „
12·5 „	17·5 „	15·6 „
From external condyle		
5·0 cm.	17·8 „	15·6 „
7·5 „	16·5 „	13·6 „
10·0 „	14·3 „	12·0 „

He could perform any movement with his left arm or forearm, though less powerfully than with his right; but in the left hand there was no movement of the small muscles of the thumb, of the interossei, or of the little finger.

The left trapezius was not affected. The deltoid, rhomboid, supraspinatus, infraspinatus, and pectorals were all slightly affected. All the muscles of the upper and lower arm were working but not strongly, especially the flexors of the upper arm and the extensors of the forearm. Below the wrist none of the small muscles were acting at all.

All the muscles of the arm and forearm reacted well to faradism, but none of the small muscles of the hand responded to this stimulus. The small muscles of the thenar and hypothenar eminences reacted well to 5 ma. of galvanic current; the interossei also reacted to the same strength of current, but more slowly. In all cases, however, the contraction caused on closing the current was greater when stimulated by the kathode than by the anode.

The reflexes were obtained and were normal.

Sensation was not affected.

Case VI—.Aged 10, *sister of Cases V. and VII. September* 10, 1908, *had headache, dry, troublesome cough, and pain in suboccipital region when moved. September* 13 *had lost all power in her neck. Partially recovered in ten days, but was three weeks before could hold her head up for any length of time. Examined February*, 1909, *and nothing abnormal found.*

Eva Rose M. had been away with the rest of the family to Gatestown and had returned to Upminster on September 3. On September 10, one day after her brother Stanley (Case V.) had been taken ill, she had a bad headache, a dry, troublesome cough, with hot sweats and severe pain in the suboccipital region on movement. She did not vomit and had no rash. On September 13 she had lost all power in her neck. There was no wasting and both sides appeared to be affected equally. In ten days she had partially recovered, but for about three weeks could not hold up her head for long at a time.

Condition in February, 1909.—Like the rest of the family, she is rather small for her age. She had had the usual infantile complaints, but since five years of age has been quite well. She said that at times (for instance, when cold) her neck felt rather weak, but there was nothing abnormal to be seen or detected either in her neck or in any other part of her body.

Case VII.—Aged 6, *sister of Cases V. and VI. September* 12, 1908, *had a bad headache, vomiting, feverishness, and general malaise. September* 14 *had entirely lost the use of both lower extremities. Gradually recovered the use of the left leg, but the right never quite recovered. When examined in February*, 1909, *the left leg was not obviously affected, but there was flaccid paralysis of most muscles of the right thigh.*

Family History.—Gladys was the third of the M. family to be taken ill, two days after her sister Eva Rose (Case VI.) and three days after her

brother Stanley (Case V.). The eldest and youngest were never affected, though exposed apparently to equal risk of infection.

Condition in February, 1909.—A bright, plump child of moderate size for her age, and a good colour. She has had no previous illnesses. The muscles of the right thigh were obviously wasted and lacked tone. The muscles of the right leg and of the left thigh and leg appeared perfectly normal.

There were no cutaneous or vasomotor changes.

Below the patella both legs were equal; above the patella the right leg was the smaller.

Above patella	*Right*	*Left*
5·0 cm.	23·8 cm.	26·6 cm.
7·5 „	25·4 „	29·3 „
10·0 „	27·0 „	30·5 „

She walked and ran without any limp, difficulty, or unsteadiness. She could perform any movement, but there was not so much power in the right thigh as in the left.

The right quadriceps was very weak, the rectus and vastus externus not acting at all. The adductors and hamstring acted moderately, the biceps appearing to be the most affected of the hamstrings. All other muscles of both lower extremities acted well.

The right rectus did not react at all to the faradic current; the right vastus internus reacted badly. All the other muscles reacted well to the faradic current. All the muscles, including the rectus, reacted normally to a galvanic current of 5 ma.

The knee-jerk was stronger on the left side, but was present on the right. On both sides the plantar reflex was flexor.

There were no sensory changes.

Case VIII.—Aged 13, *without any constitutional symptoms, was paralysed in his right leg on September* 16, 1908. *In eight days was quite well. Examined February*, 1909, *and nothing abnormal found.*

Basil J. had been away at Bexhill during August and had returned to Upminster on August 31. On September 10 he was kicked in the lumbar region by a man. The kick was not severe. He went to bed quite well, and went to school next day. On the following morning, September 12, he fell down when he got out of bed, owing to weakness of his right leg. He was examined by Dr. Dunlop. He was in no way ill; he had no cough, no sore throat, and no pain. There was no knee-jerk in the right leg; the muscles were flaccid, and there was no movement below the knee. There was no bruising of the spine. After three or four days he began to improve, and in eight days was quite well.

He has an older and a younger brother, both of whom were at home at the time of his illness, but they remained quite well.

Condition in February, 1909.—He was a fine, muscular boy in excellent health, and he had never had any serious illness. There was no weakness nor loss of tone of the right leg. Measurements showed the right leg to be slightly larger than the left. The knee-jerks were equal on both sides, and there were no vasomotor changes.

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Publications Recently Received.

[*Notes on a book under this heading do not preclude a subsequent review.*]

Syphilis and Nervensystem. (Neunzehn Vorlesungen für praktische Aerzte, Neurologen und Syphilidologen.) Von Dr. Max Nonne. Zweite vermehrte und erweiterte Auflage. Mit 97 Abbildungen im Text. S. 699. Berlin: Karger, 1909.

Syphilis (as manifested by its effects on the nervous system) is here treated in the fullest manner. Each lecture forms a chapter dealing with one aspect of the subject, illustrated with admirable clinical cases. Professer Nonne first deals with the nature of syphilis in the light of modern research, and then gives a full description of the anatomical appearances produced by the disease in the nervous system. He then passes on to arteritis and its effects, to meningitis of the superior surface of the brain and of the base, including lesions of the cranial nerves. The neuroses and psychoses of syphilis are described and are distinguished from dementia paralytica. Three lectures are devoted to various conditions of the spinal cord and its membranes due to syphilis. Tabes and its relation to syphilis is fully considered, and this is followed by an interesting account of cerebrospinal syphilis. Chapters on hereditary syphilitic nervous disease, on treatment, on cyto-diagnosis, and on Wassermann's reaction complete this most valuable work. Its admirable arrangement and its completeness make it an ideal reference book for the practical neurologist.

Klinische Beiträge zur Lehre von der Hysterie nach Beobachtungen aus dem Nordwesten Russlands. Von Dr. Georg Voss. S. 300. Jena: Fischer, 1909.

The author studied 123 cases of hysteria which came to the Marien hospital in Petersburg, and on this material has based a useful clinical monograph. Chapters are devoted to alterations in sensibility, the reflexes, the special senses, vasomotor and trophic changes, and affections of motility. The work of others is invariably considered, and the views of the author are in accord with those of most neurologists. Thus he does not believe that the sensory disturbances and the limitation of the visual field are phenomena suggested by medical examination, and looks upon them as of diagnostic importance.

The Criminal Responsibility of Lunatics: a Study in Comparative Law. By HEINRICH OPPENHEIMER, LL.D., M.D. Pp. 275. London: Sweet and Maxwell, 1909.

This work is an attempt to bridge the gulf between legal and medical opinion on criminal responsibility by one who is both a lawyer and a medical man. Chapters are devoted not only to the English law, but to a careful survey of the laws of other countries, and the author describes the actual working of the paragraphs on criminal responsibility in the various European States. The "knowledge test," freedom of will, and the power of self-control are fully dealt with. The treatment of moral insanity, partial insanity, and "the critical moment" is less complete, probably because they require wide clinical knowledge and familiarity with actual examples of the conditions described. This book is an interesting attempt to deal with a subject rendered difficult by the fundamental difference in outlook of lawyers and medical men.

Attention. By W. B. PILLSBURY. Pp. 346. London: Swan Sonnenschein, 1908.

This work formed originally one of the volumes of "The Bibliothèque Internationale de Psychologie expérimentale," and the present volume is a republication with numerous additions. It contains an account of all the recent methods for studying attention and the results obtained by their use. Attention is treated physiologically, psychologically, and philosophically. Chapters are devoted to the relation of attention to ideas, perception, memory, will, reason, and feeling. Every chapter concludes with a useful summary, and the book forms a valuable record of our present knowledge of this difficult subject.

Jahresbericht über die Leistungen und Fortschritte auf dem Gebiete der Neurologie und Psychiatrie. XII. Jahrgang: Bericht über das Jahr, 1908. S. 1312. Berlin: G. Karger, 1909.

This volume retains all the excellences of previous numbers. No working neurologist can afford to be without this work of reference on his shelves.

A Text-book of Mental Disease. By EUGENIO TANZI. Authorized translation from the Italian by W. FORD ROBERTSON, M.D., C.M., and T. C. MACKENZIE, M.D., F.R.C.P. Pp. 803. London: Rebman, 1909.

This is a well-arranged text-book on clinical lines. The illustrations are good and the translation excellent.

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